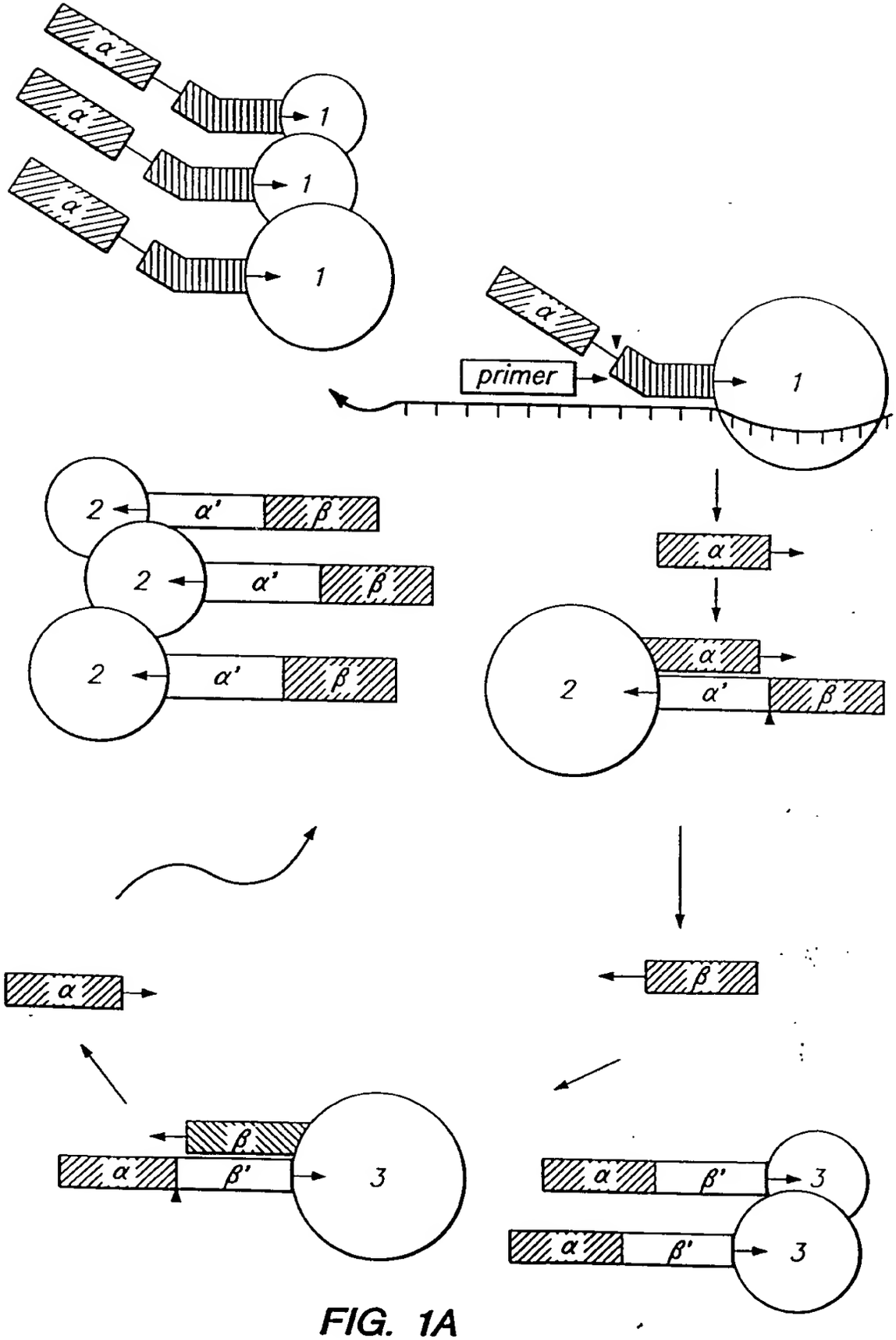


FIG. 1A

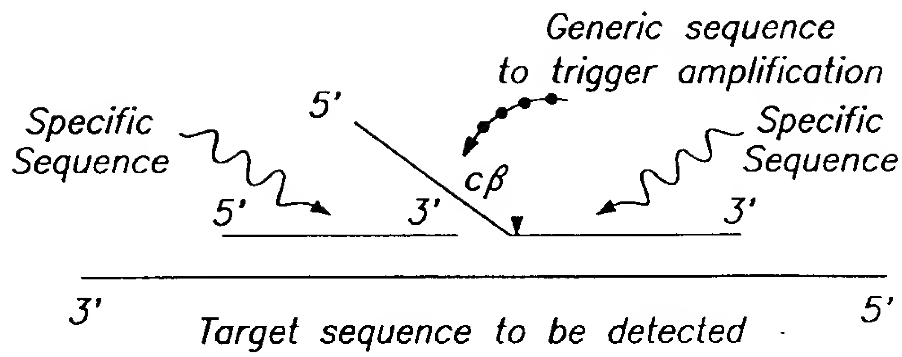


FIG. 1B PART ONE: TRIGGER REACTION

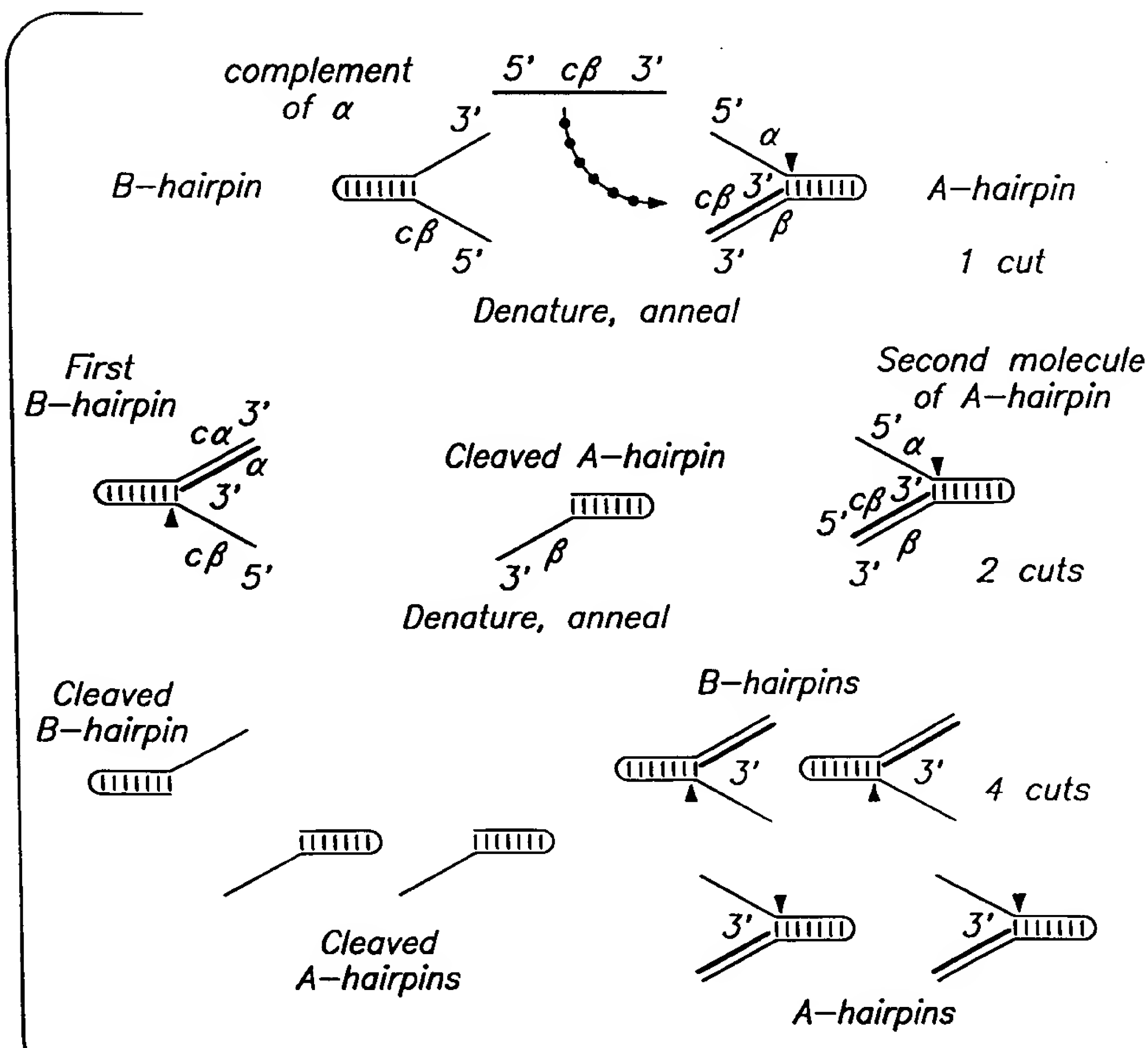


FIG. 1C PART TWO: DETECTION REACTION

```
MAJORITY ATGXXGGCGATGCTTCCCCTCTTTGAGCCCAAAGGCCGGGTCCTCCTGGTGGACGGGCACCACCTGGCCT

DNAPTAQ  ...AG..G.....G.................G.....................................  70
DNAPTFL  ..........................................C..G.....................  67
DNAPTTH  ...GA...........G.......A.....................................  70

MAJORITY ACCGCACCTTCTTCGCCCTGAAGGGCCTCACCACCACCOGGGGGGAACCGGTGCAGGCGGTCTACGGCTT

DNAPTAQ  ..........CA.....................................G..G.....................  140
DNAPTFL  ............T.....C.....................C........C..T.....................  137
DNAPTTH  ..................................G.....................................  140

MAJORITY CGCCAAGAGCCTCCTCAAGGCCCTGAAGGAGGACGGGGACXXGCCGGTGXTCGTGGTCTTTGACGCCAAG

DNAPTAQ  ........................C.....................A.....................  207
DNAPTFL  ......A.....................................GT..T.....................  204
DNAPTTH  ..........................................T..AA...C..CT.....................  280

MAJORITY GCCCCCTCCTTCCGCCACGAGGCCTACGAGGCCTACAAGGCGGGCCGGGCCCCCACCCCGGAGGACTTTC

DNAPTAQ  ............................G..GG.....................G.....................  277
DNAPTFL  ..............................................................................  274
DNAPTTH  ..........................................GA.......G.....C........C.  280

MAJORITY CCCGGCAGCTCGCCCTCATCAAGGAGCTGGTGGACCTCCTGGGGCTTGCGCGCCTCGAGGTCCCCGGCTA

DNAPTAQ  .......A.....................................G.................G.....  347
DNAPTFL  ..........G.............T.............A..C....T...G..G.....T.......T  344
DNAPTTH  ..........................................T..A.C.....................  350
```

FIG. 2A

```
MAJORITY CGAGGCGGACGACGTXCTGGCCACCCTGGCCAAGAAGGCGGAAAAGGAGGGGTACGAGGTGCGCATCCTC

DNAPTAQ  ..............C.......G.............................C........C.........  417
DNAPTFL  T.............G.................CG.....................................  414
DNAPTTH  ..............T..C.....................................................  420

MAJORITY ACCGCCGACCGCGACCTCTACCAGCTCCTTTCCGACCGCATCGCCGTCCTCCACCCCGAGGGGTACCTCA

DNAPTAQ  .........AAA....T.........................CA............................  487
DNAPTFL  ..T.............................G..G.........A.........T...........G.  484
DNAPTTH  ......................A...G.C.........G.....................CC.......  490

MAJORITY TCACCCCGGCGTGGCTTTGGGAGAAGTACGGCCTGAGGCCGGAGCAGTGGGTGGACTACCGGGCCCTGGC

DNAPTAQ  .........C...........A.................C..C.......CC..............A.  557
DNAPTFL  ..................AC..............C.C.................................  554
DNAPTTH  .........A.........................C.....................T...C.....C.T  560

MAJORITY GGGGGACCCCTCCGACAACCTCCCCGGGGTCAAGGGCATCGGGGAGAAGACCGCCCXGAAGCTCCTCXAG

DNAPTAQ  C......GAG...........T.............................G..GAG......T..GG..  627
DNAPTFL  ............G..T...A.........G.....................A..G....A..CGC  624
DNAPTTH  ..................................................TC.........A..  630

MAJORITY GAGTGGGGGAGCCTGGAAAACCTCCTCAAGAACCTGGACCGGGTGAAGCCCGC···CXTCCGGGAGAAGA

DNAPTAQ  ..................GC.....................C.............A.............  694
DNAPTFL  .....................T..C..C.........A.........T.....T.G.........C  691
DNAPTTH  ........A.....................................A.....A.AAAA.G.........  700
```

FIG. 2B

```
MAJORITY TCCAGGCCCACATGGAXGACCTGAXGCTCTCCTGGGAGCTXTCCCAGGTGCGCACCGACCTGCCCCTGGA

DNAPTAQ  ...T...........C..T....A...........C..GG..A.......................... 764
DNAPTFL  .......GGG......G.C....GCC..T...C..A....T.........A...T.............. 761
DNAPTTH  ..A........C....A.....C.G........T......C....G..............C........ 770

MAJORITY GGTGGACTTCGCCAAGXGGCGGGAGCCCGACCGGGAGGGGCTTAGGGCCTTTCTGGAGAGGCTGGAGTTT

DNAPTAQ  ..............AA.....................A.........................T..... 834
DNAPTFL  ..........GG.G.C.C..CACA...A...T......T..GC....T...T.....C..T........ 831
DNAPTTH  .......C.....C..G.....................................C..............C 840

MAJORITY GGCAGCCTCCTCCACGAGTTCGGCCTCCTGGAGGGCCCCAAGGCCCTGGAGGAGGCCCCCTGGCCCCCGC

DNAPTAQ  ........................T.....AA..................................... 904
DNAPTFL  ..A.............................G..G.....GGCA.....................T. 901
DNAPTTH  ..............................C....GCCC.............................. 910

MAJORITY CGGAAGGGGCCTTCGTGGGCTTTGTCCTTTCCCGCCCCGAGCCCATGTGGGCCGAGCTTCTGGCCCTGGC

DNAPTAQ  ........................G.........AAG.................T.............. 974
DNAPTFL  ..........T..TT........TC.T.......T.................................. 971
DNAPTTH  ......................C.....C.....................G......AAA........ 980

MAJORITY CGCCGCCAGGGAGGGCCGGGTCCACCGGGCACCAGACCCCTTTAXGGGCCTXAGGGACCTXAAGGAGGTG

DNAPTAQ  ..........G..................C..C..G..T.A..AA.C...C........G.......C. 1044
DNAPTFL  T.GG..GT.......G..CC....T.......A.......C...G......G........T....G.... 1041
DNAPTTH  ....TG......C........G.........G..........GGC...G..A.A......C........C 1050
```

FIG. 2C

```
MAJORITY CGGGGXCTCCTCGCCAAGGACCTGGCCGTTTTGGCCCTGAGGGAGGGCCTXGACCTCXTGCCCGGGGACG

DNAPTAQ  .....G..T........A......AG....C.............A.....T.G....CC......C.... 1114
DNAPTFL  .....AA....G.............G.............C.........G......T.C..A.A..... 1111
DNAPTTH  .....C.................C.....C......TC.........G..A......G.............. 1120

MAJORITY ACCCCATGCTCCTCGCCTACCTCCTGGACCCCTCCAACACCACCCCCGAGGGGGTGGCCCGGCGCTACGG

DNAPTAQ  ................................T.......................................... 1184
DNAPTFL  ...........G.........T.........................T.................T..... 1181
DNAPTTH  ..................................................G.......... 1190

MAJORITY GGGGGAGTGGACGGAGGAXGCGGGGGAGCGGGCCCTCCTXTCCGAGAGGCTCTTCCXGAACCTXXXGGAG

DNAPTAQ  C.................G..............GC...T..............GCC.....GTG..G. 1254
DNAPTFL  .................T.........A.........GG.....C.C.......A..C...AAA.... 1260
DNAPTTH  .................C..C.CCC.C...........C..G.........CAT.G......CCTTA.. 1260

MAJORITY CGCCTTGAGGGGGAGGAGAGGCTCCTTTGGCTTTACCAGGAGGTGGAGAAGCCCCTTTCCCGGGTCCIGG

DNAPTAQ  A.G.....................................G..........G..........GCT....... 1324
DNAPTFL  .....A....A..A..AC.C..G............G................G............GT... 1321
DNAPTTH  .....C.............A............C.....C........A........C.............. 1330

MAJORITY CCCACATGGAGGCCACGGGGGTXCGGCTGGACGTGGCCTACCTCCAGGCCCTXTCCCTGGAGGTGGCGGA

DNAPTAQ  .....................G..C.............T...AG....T.G.............C.. 1394
DNAPTFL  ...GG.................C.....................C.............A..C 1391
DNAPTTH  ...............C.....A.....................T........T.........C.T..... 1400
```

FIG.2D

```
MAJORITY  GGAGATCCGCCGCCTCGAGGAGGAGGTCTTCCGCCTGGCCGGCCACCCCTTCAACCTCAACTCCCGGGAC

DNAPTAQ   .......GC...........CC........................................  1464
DNAPTFL   ....G.G....AG..G..................................................C...  1461
DNAPTTH   ..................................T....G..............................  1470

MAJORITY  CAGCTGGAAAGGGTGCTCTTTGACGAGCTXGGGCTTCCCGCCATCGGCAAGACGGAGAAGACXGGCAAGC

DNAPTAQ   ..............C..............A................................C.......  1534
DNAPTFL   ........GC...................G..C..G..T.......................G..G..A.  1531
DNAPTTH   .............................TA...........T.G..G......C.A.....A.......  1540

MAJORITY  GCTCCACCAGCGCCGCCGTGCTGGAGGCCCTXCGXGAGGCCCACCCCATCGTGGAGAAGATCCTGCAGTA

DNAPTAQ   ...................C...........C..C...................................  1604
DNAPTFL   .............T.................G..A....................CCGC...........  1601
DNAPTTH   ................G..............A..G.............................C...C.  1610

MAJORITY  CCGGGAGCTCACCAAGCTCAAGAACACCTACATXGACCCCCTGCCXGXCCTCGTCCACCCCAGGACGGGC

DNAPTAQ   ..................G....G.........T......T....G.A....A.................  1674
DNAPTFL   .................................A...........C.C...G..........A...C...  1671
DNAPTTH   ...............................G.G...........AAG............G.........  1680

MAJORITY  CGCCTCCACACCCGCTTCAACCAGACGGCCACGGCCACGGGCAGGCTTAGTAGCTCCGACCCCAACCTGC

DNAPTAQ   ...............................................A...........T........C.  1744
DNAPTFL   ..G.............................C...............TCC...................  1741
DNAPTTH   .........................................G............................  1750
```

FIG. 2E

```
MAJORITY AGAACATCCCCGTCCGCACCCCXCTGGGCCAGAGGATCCGCCGGGCCTTCGTGGCCGAGGAGGGXTGGGT

DNAPTAQ  .....................G..T..G.....................A.C..........G...C.  1814
DNAPTFL  ............G.......T.........C.C.......A.....................C.....  1811
DNAPTTH  .....................CT.....................................C...T....C  1820

MAJORITY GTTGGTGGCCCTGGACTATAGCCAGATAGAGCTCCGGGTCCTGGCCCACCTCTCCGGGGACGAGAACCTG

DNAPTAQ  A.....................................A....G.................C.........  1884
DNAPTFL  .C......T.T.......C........T.....T.....................................  1881
DNAPTTH  .....................................C.....C.....................A.....  1890

MAJORITY ATCCGGGTCTTCCAGGAGGGGAGGGACATCCACACCCAGACCGCCAGCTGGATGTTCGGCGTCCCCCCGG

DNAPTAQ  .....................C.............GG.....................................G..  1954
DNAPTFL  ...........T.....................................................TT....C.  1951
DNAPTTH  ...A.................A.....................A.....................  1960

MAJORITY AGGCCGTGGACCCCCTGATGCGCCGGGCGGCCAAGACCATCAACTTCGGGGTCCTCTACGGCATGTCGGC

DNAPTAQ  .....................................................................G..  2024
DNAPTFL  .A.GG..A.....T.....................................G.....................  2021
DNAPTTH  ...................................GG.G.......C.....................  2030

MAJORITY CCACCGCCTCTCCCAGGAGCTTGCCATCCCCTACGAGGAGGCGGTGGCCTTCATTGAGCGCTACTTCCAG

DNAPTAQ  .....................A........T..........CCA.....................T...  2094
DNAPTFL  ............GG......T.....................................................  2091
DNAPTTH  ...TA.G.....................................T..A.............A  2100
```

FIG. 2F

```
MAJORITY AGCTTCCCCAAGGTGCGGGCCTGGATTGAGAAGACCCTGGAGGAGGGCAGGAGGCGGGGTACGTGGAGA

DNAPTAQ  .....................................................................  2164
DNAPTFL  ....A........................GG......C.........C.CC..........T.......  2161
DNAPTTH  ..........................A..A................G....A......C........A.  2170

MAJORITY CCCTCTTCGGCCGCCGGCGCTACGTGCCCGACCTCAACGCCCGGGTGAAGAGCGTGCGGGAGGCGGCGGA

DNAPTAQ  ...............C...........A.....AG.G.............................C..  2234
DNAPTFL  .....................T...................................C...........  2231
DNAPTTH  ..........AA.AA.......................................CA.......C.....  2240

MAJORITY GCGCATGGCCTTCAACATGCCCGTCCAGGGCACCGCCGCCGACCTCATGAAGCTGGCCATGGTGAAGCTC

DNAPTAQ  ........................................................T............  2304
DNAPTFL  .....................G.........................................CG...T  2301
DNAPTTH  .....................................................C...............  2310

MAJORITY TTCCCCCGGCTXCAGGAAATGGGGGCCAGGATGCTCCTXCAGGTCCACGACGAGCTGGTCCTCGAGGCCC

DNAPTAQ  ......A....GG........................T...............................  2374
DNAPTFL  ...........T......C.......G.......TT.G.....G.........................  2371
DNAPTTH  ........C..C.G...G........C.C........C.................CC....G.......  2380

MAJORITY CCAAAGAGCGGGCGGAGGXGGTGGCCGCTTTGGCCAAGGAGGTCATGGAGGGGGTCTATCCCCTGGCCGT

DNAPTAQ  .A......A.........CC.....CGGC.........................G..............  2444
DNAPTFL  ....G..C........AG...A..................................GG......CAG..  2441
DNAPTTH  ..C...C......C....A......G...............C.......AA..C.........C.....  2450
```

FIG. 2G

```
MAJORITY GCCCCTGGAGGTGGAGGTGGGGATGGGGGAGGACTGGCTCTCCGCCAAGGAGTAG

DNAPTAQ  .........................A.............................GA   2499
DNAPTFL  ......................CC..................................   2496
DNAPTTH  ....................................T.........GT...        2505
```

FIG. 2H

```
MAJORITY MXAMLPLFEPKGRVLLVDGHHLAYRTFFALKGLTTSRGEPVQAVYGFAKSLLKALKEDG·DAVXVVFDAK

TAD PRO  .RG.....H.....I.....  69
TFL PRO  .·.....V.V.....  68
TTH PRO  .E.....YK..F.....  70

MAJORITY APSFRHEAYEAYKAGRAPTPEDFPROLALIKELVDLLGLXRLEVPGYEADDVLATLAKKAEKEGYEVRIL

TAG PRO  .....GG.....A.....S.....  139
TFL PRO  .....V.....F.....R.....  138
TTH PRO  .....FT.....  140

MAJORITY TADRDLYQLLSDRIAVLHPEGYLITPAWLWEKYGLRPEQWVDYRALXGDPSDNLPGVKGIGEKTAXKLLX

TAG PRO  ...K.....H.....D..A....T..E.....R...E  209
TFL PRO  .....E...I.....Y.....A.....I.....QR.IR  208
TTH PRO  .....V...V.....H....E.....F...V.....L...K  210

MAJORITY EWGSLENLLKNLDRVKP·XXREKIXAHMEDLXLSXXLSXVRTDLPLEVDFAXRREPDREGLRAFLERLEF

TAG PRO  .....A.....L..·AI....L...D..K..WD.AK.....K.....R.....  278
TFL PRO  .....FQH..Q...·SL...LQ.G..A.A..RK..Q.H.....GR..T.NL.....  277
TTH PRO  .....ENV....K..L...R..LE..R.....L.QG.....  280

MAJORITY GSLLHEFGLLEXPKALEEAPWPPPEGAFVGFVLSRPEPMWAELLALAAARXGRVHRAXDPLXGLRDLKEV

TAG PRO  .....S.....K.....D.....PE.YKA.....A  348
TFL PRO  .....G...A.....L..SF.....G.WE..L...Q...R.....G.  347
TTH PRO  .....A.AP.....K....C.D.....A...A..K.....  350
```

FIG. 3A

```
MAJORITY  RGLLAKDLAVLALREGLDLXPGDDPMLLAYLLDPSNTTPEGVARRYGGEWTEDAGERALLSERLFXNLXX

TAQ PRO   ........S........G.P................................E.....A......A..WG  418
TFL PRO   ..I..............F.E..................................A....QT.KE  417
TTH PRO   ............S......V..............................AH........HR..LK  420

MAJORITY  RLEGEERLLWLYXEVEKPLSRVLAHMEATGVRLDVAYLQALSLEVAEEIRRLEEEVFRLAGHPFNLNSRD

TAQ PRO   ............R...R...A................R..........A...A................  488
TFL PRO   ..K.........E...........R.....................EA.V.Q..................  487
TTH PRO   ......K.....H..........................L.........................  490

MAJORITY  QLERVLFDELGLPAIGKTEKTGKRSTSAAVLEALREAHPIVEKILQYRELTKLKNTYIDPLPXLVHPRTG

TAQ PROO  ..................................................S.......D.I.....  558
TFL PRO   ..............................DR..................A....K..  557
TTH PRO   ..........R...L...Q............................H..........V....S.......  560

MAJORITY  RLHTRFNQTATATGRLSSSDPNLQNIPVRTPLGQRIRRAFVAEEGWXLVALDYSQIELRVLAHLSGDENL

TAQ PRO   ..............................................I.....L......................  628
TFL PRO   .......................................................V..V...................  627
TTH PRO   ..............................................A..A.........................  630

MAJORITY  IRVFQEGRDIHTQTASWMFGVPPEAVDPLMRRAAKTINFGVLYGMSAHRLSQELAIPYEEAVAFIERYFQ

TAQ PRO   ............E.........R........................................Q........  698
TFL PRO   ......................S..G..............................G..S...............  697
TTH PRO   .......K.......................V.....................................  700
```

FIG. 3B

```
MAJORITY SFPKVRAWIEKTLEEGRRRGYVETLFGRRRYVPDLNARVKSVREAAERMAFNMPVQGTAADLMKLAMVKL

TAQ PRO  ..............................E.....................................  768
TFL PRO  .Y.....G.....................................................R.  767
TTH PRO  .....K.....................................................  770

MAJORITY FPRLXEMGARMLLQVHDELVLEAPKXRAEXVAALAKEVMEGVYPLAVPLEVEVGXGEDWLSAKEX

TAQ PRO  ....E.....................E...A..R.....................I.....  833
TFL PRO  ....Q.L.....................D...R.....W..Q.....L.....  831
TTH PRO  ....R.....................L.....QA...E.....A..KA.....M.....G  835
```

FIG. 3C

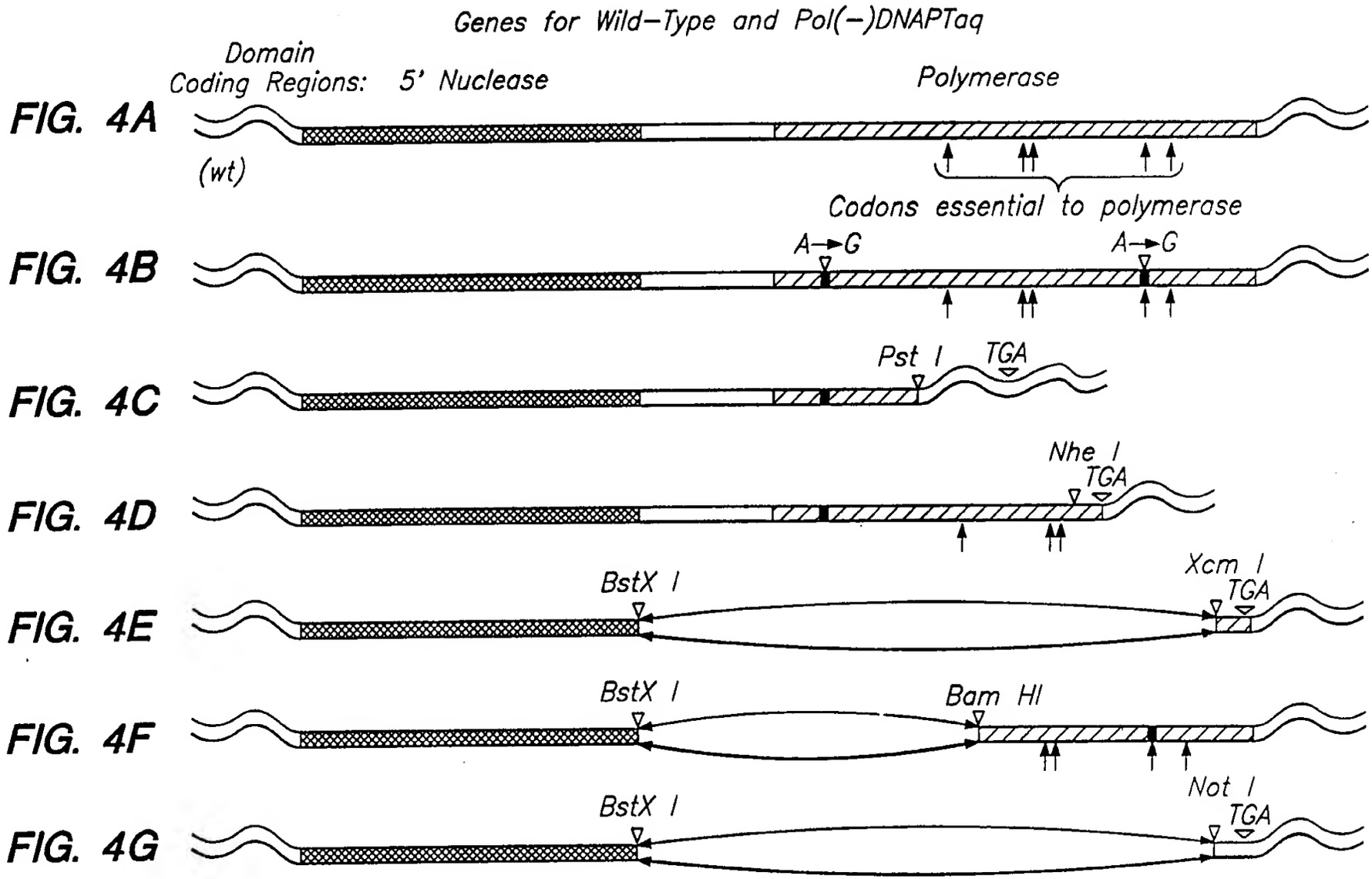


FIG. 4A

FIG. 4B

FIG. 4C

FIG. 4D

FIG. 4E

FIG. 4F

FIG. 4G

Genes for Wild-Type and Pol(–)DNAPTfl

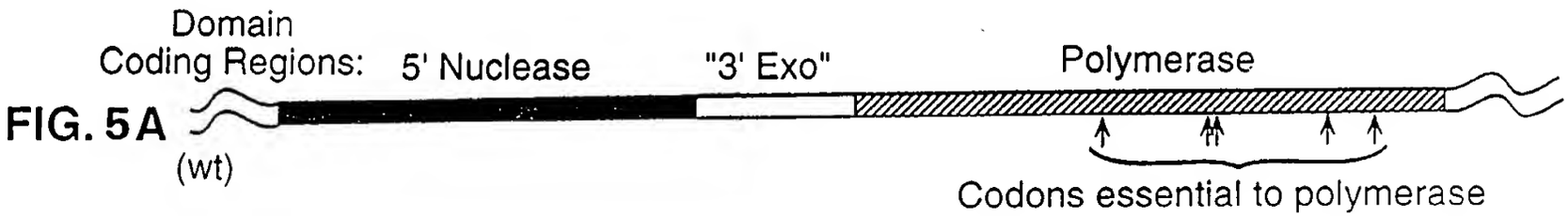


FIG. 5A

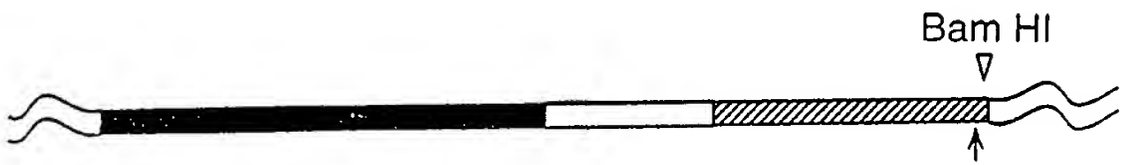


FIG. 5B

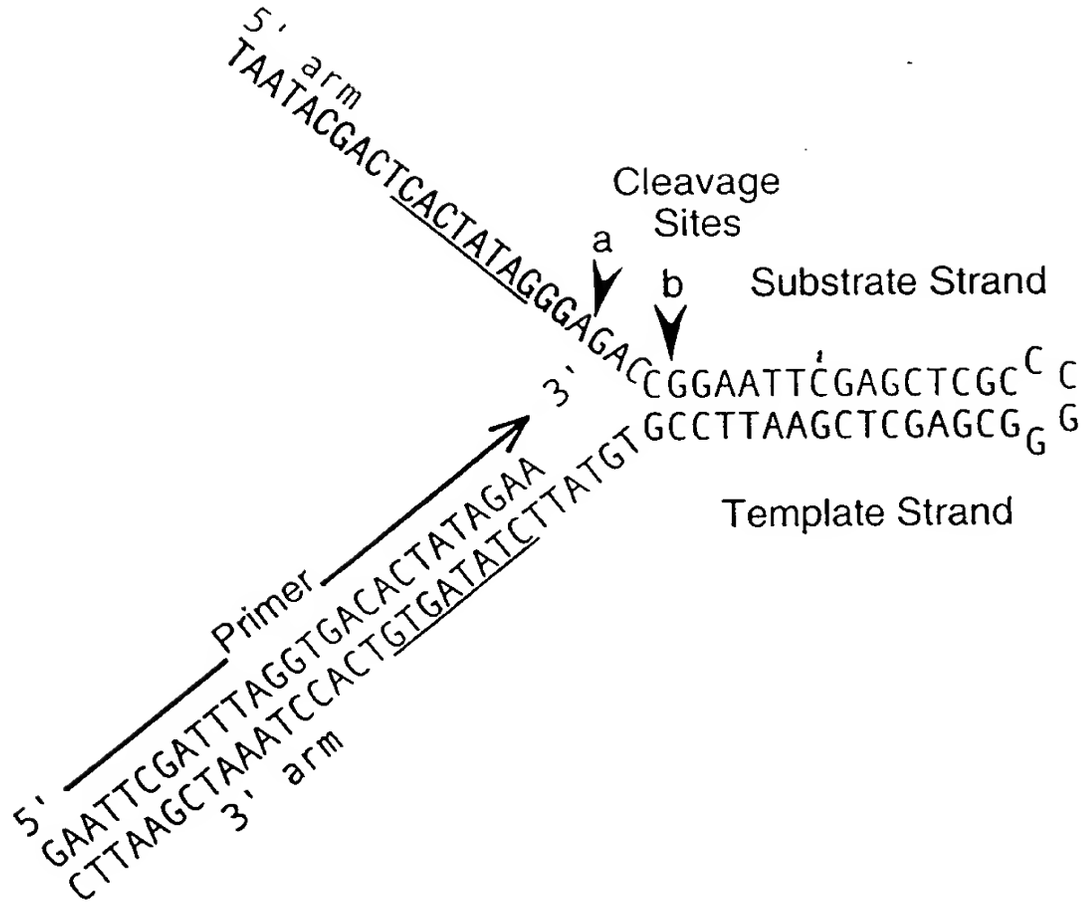

5' arm
TAATACGACTCACTATAGGGAGACC
Cleavage
Sites
a
b
Substrate Strand
3'
CGGAATTCGAGCTCGC C C
GCCTTAAGCTCGAGCG G G
Template Strand
Primer
5'
GAATTCGATTTAGGTGACACTATAGAA
CTTAAGCTAAATCCACTGTGATATCTTATGT
3' arm

FIG. 6

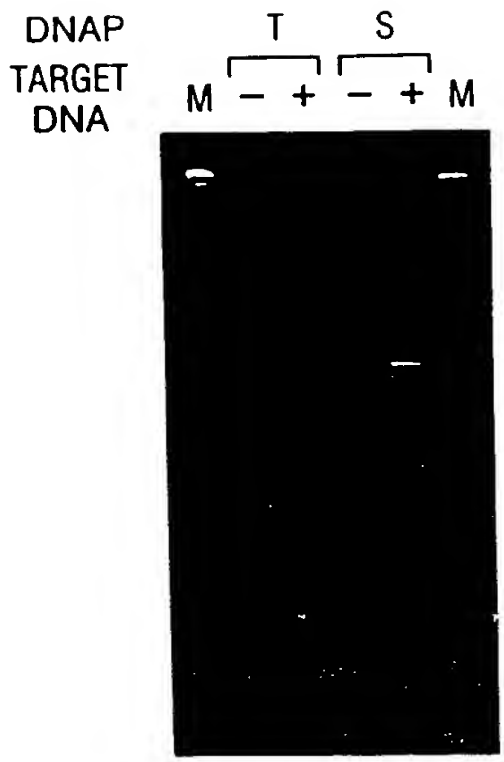


FIG. 7

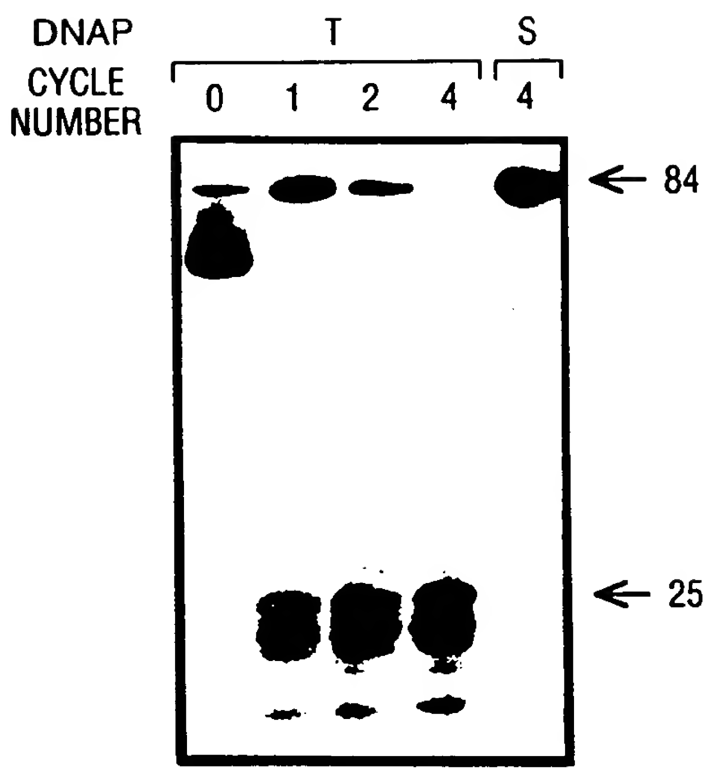


FIG. 8

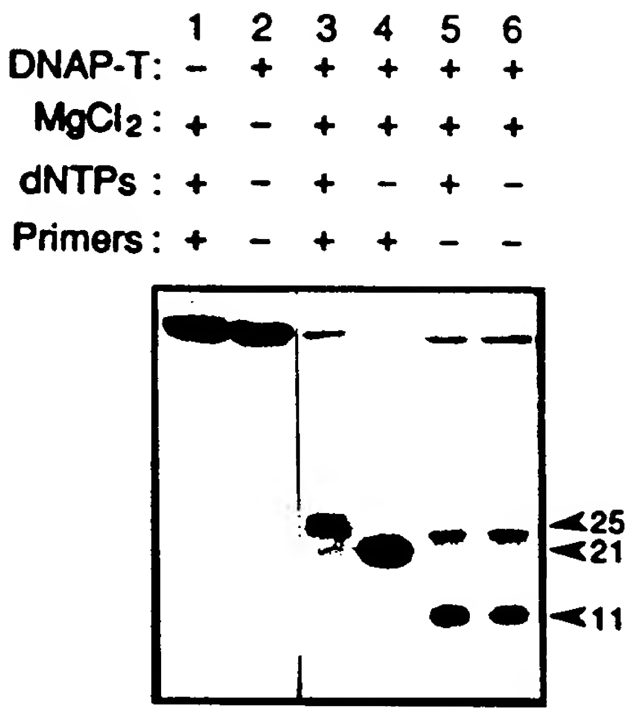


FIG. 9A

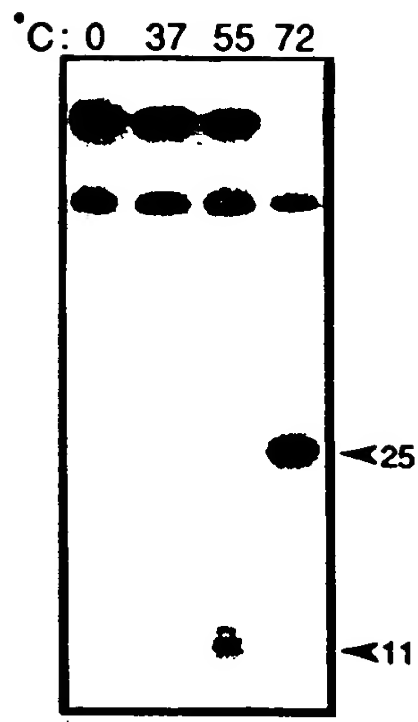


FIG. 9B

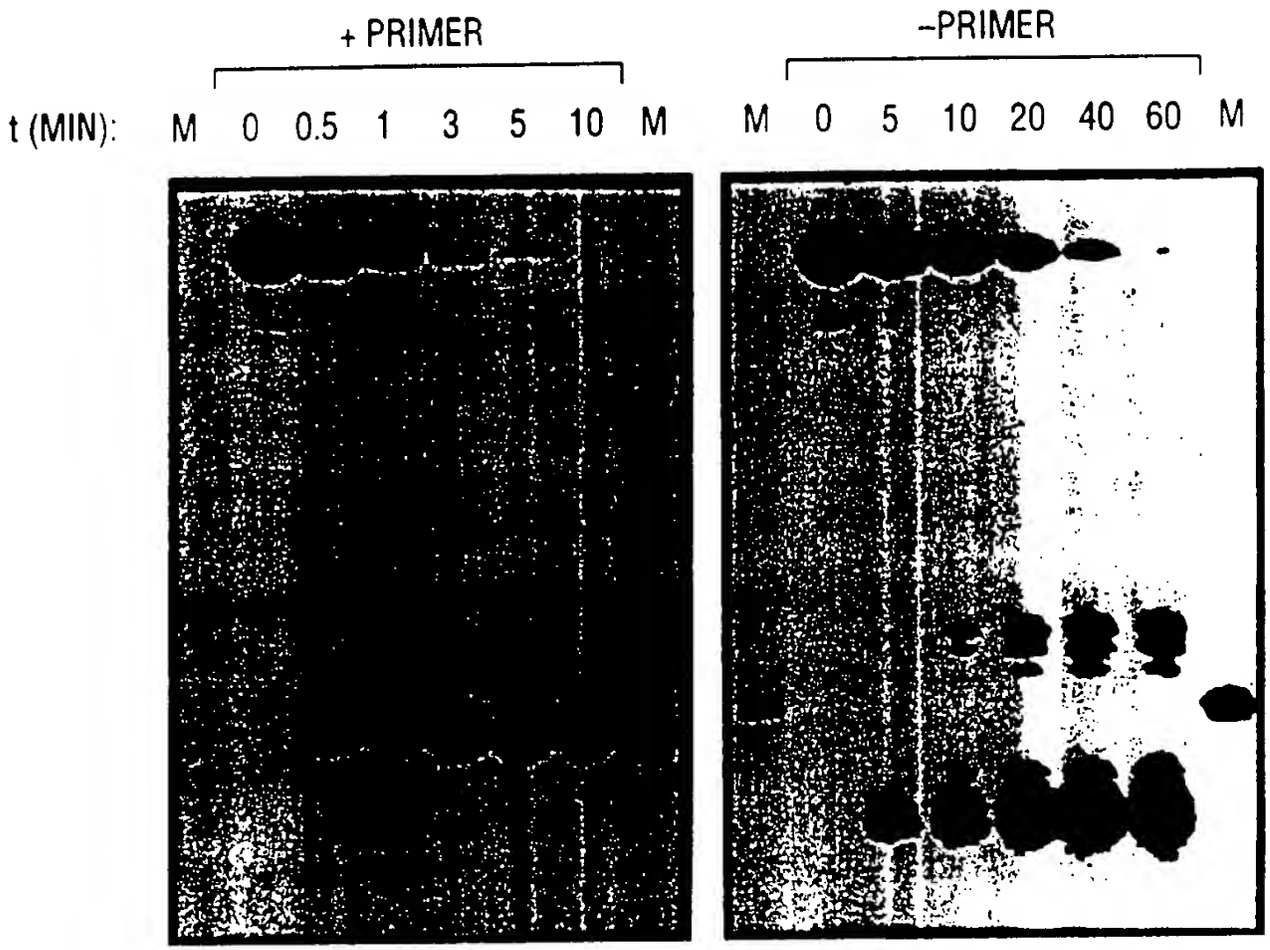


FIG. 10A

FIG. 10B

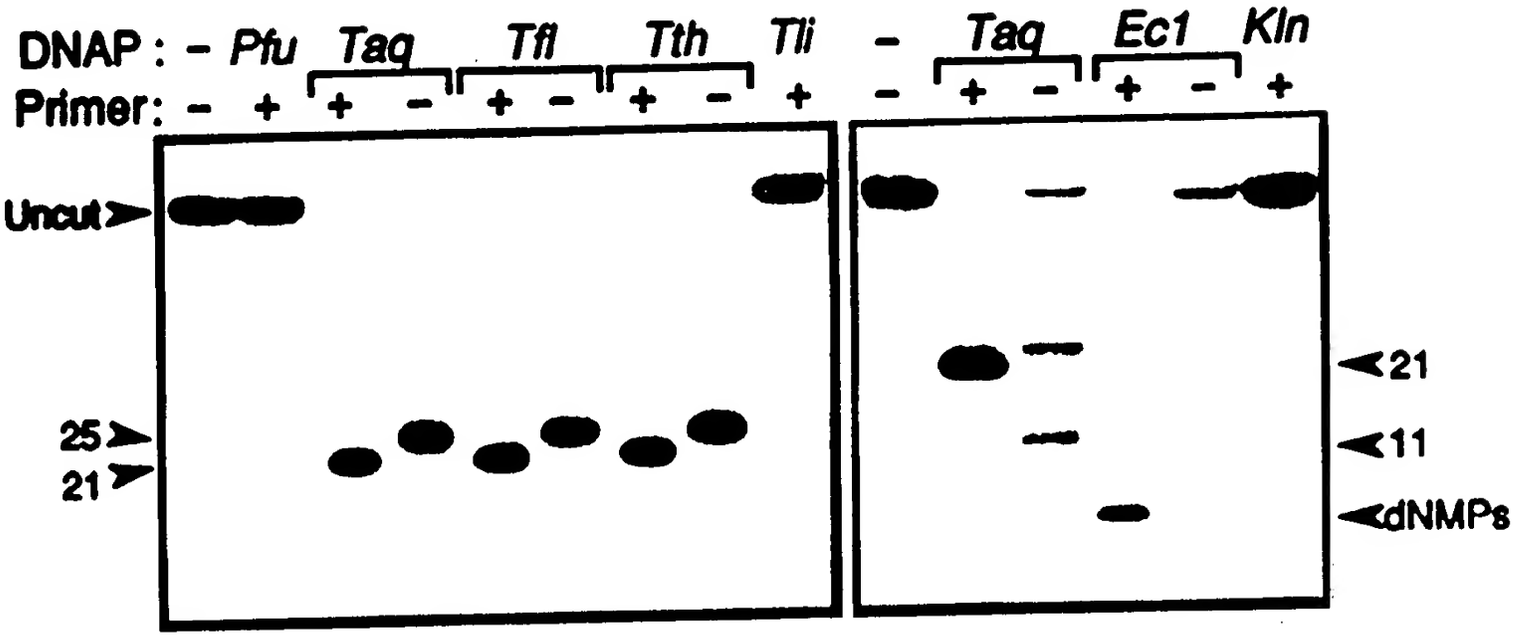


FIG. 11A

FIG. 11B

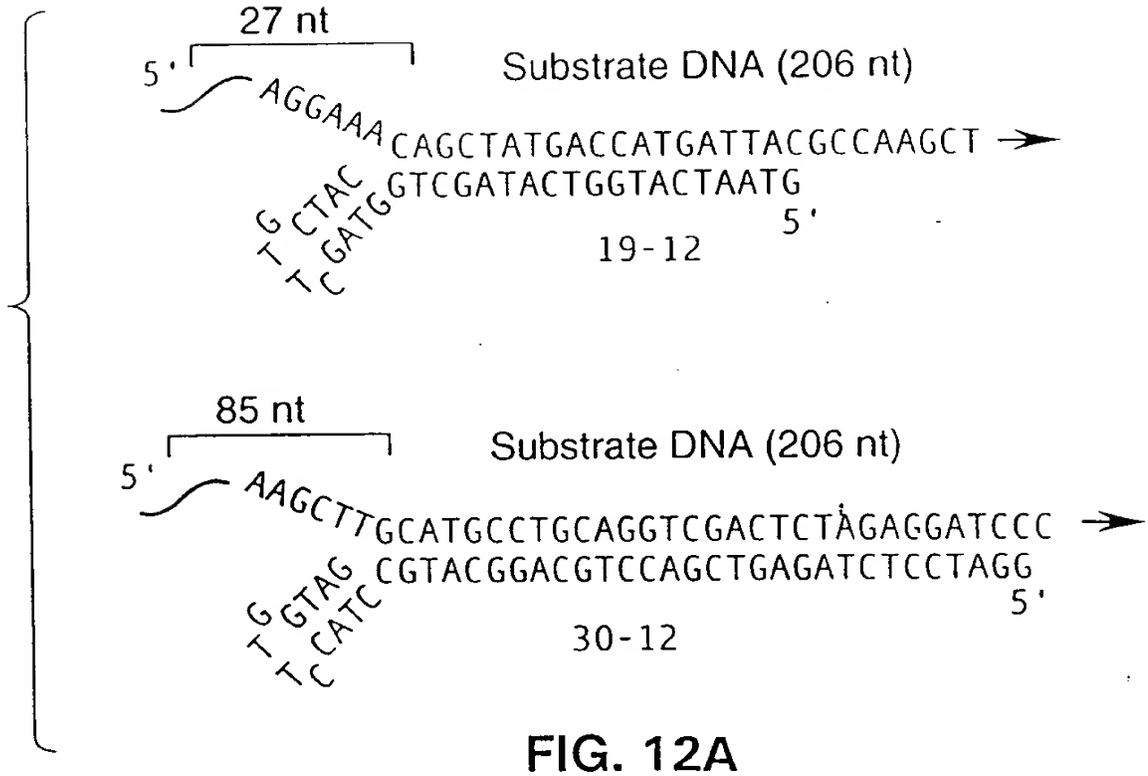


FIG. 12A

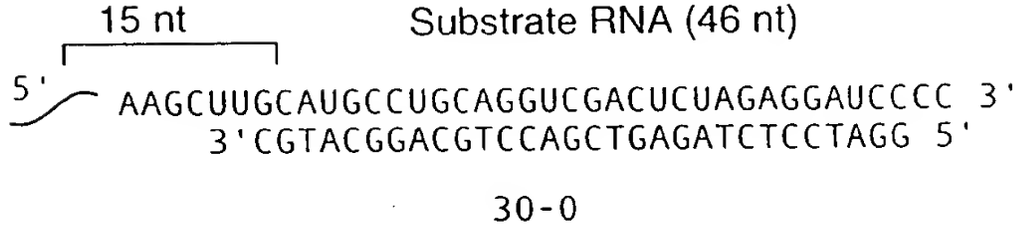


FIG. 13A

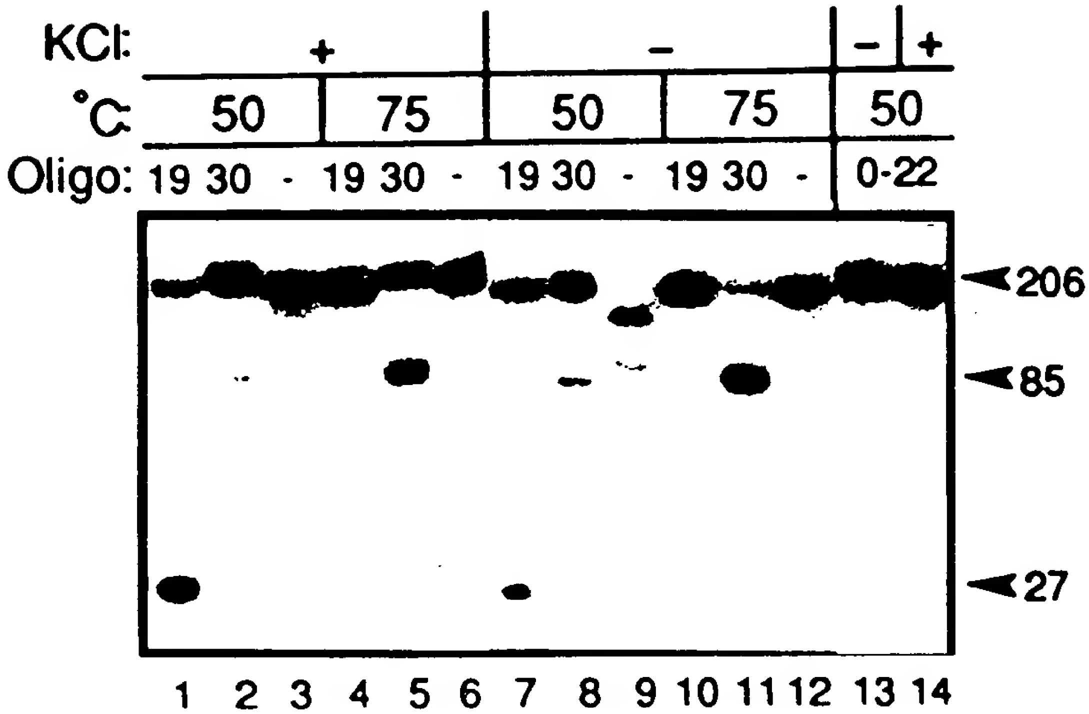


FIG. 12B

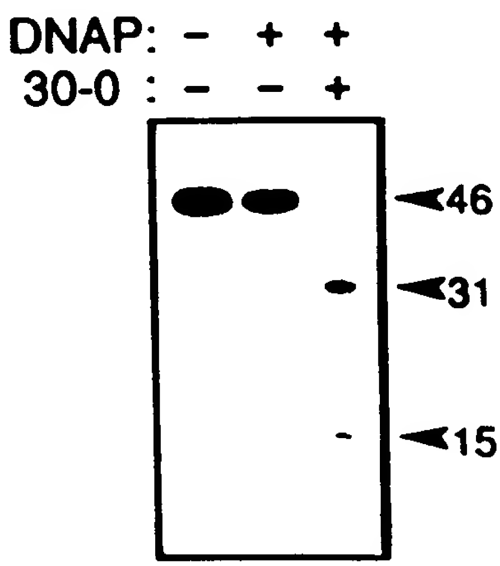
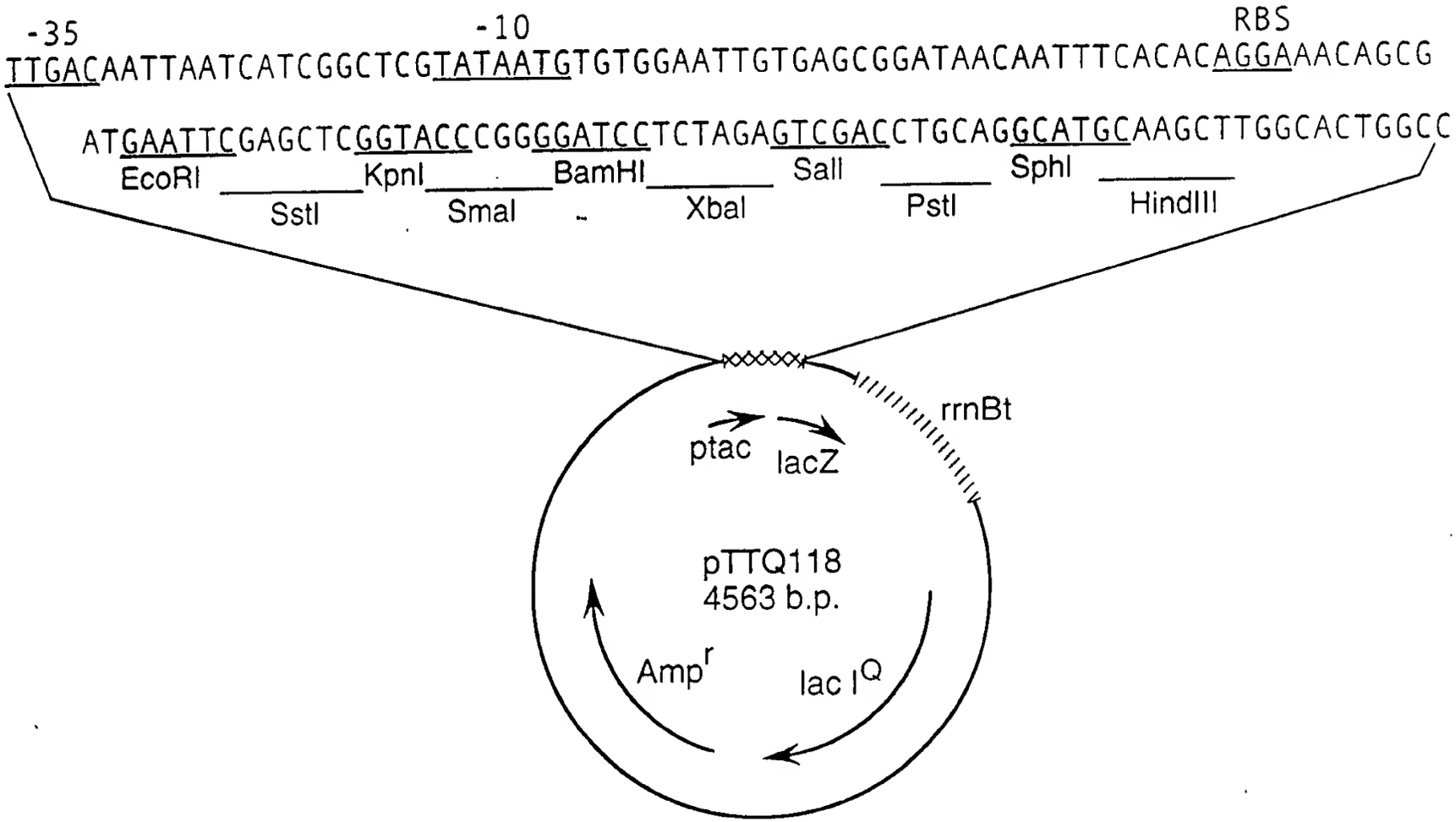
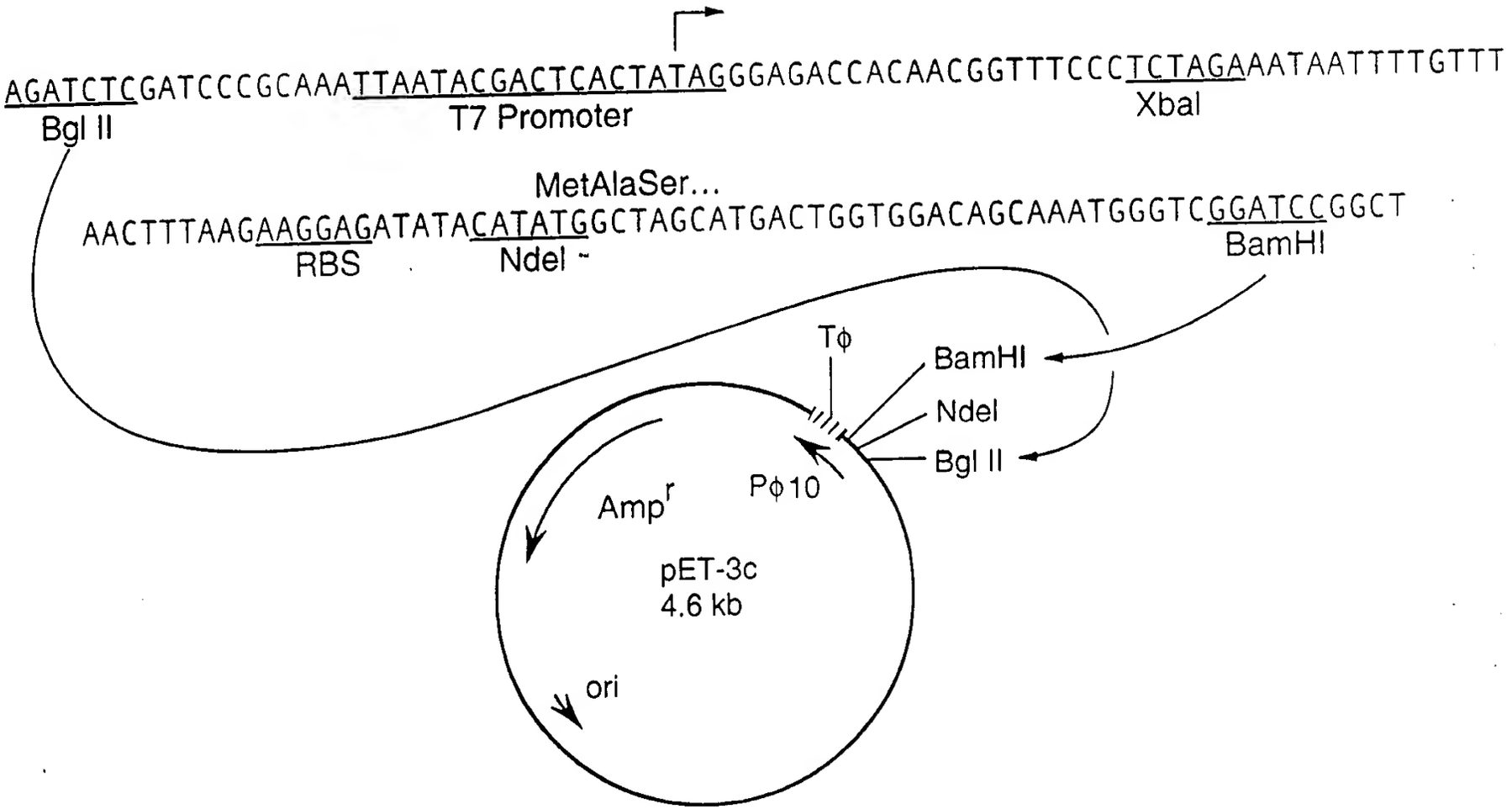


FIG. 13B



RBS: Ribosome binding site
ptac: Synthetic tac promoter
lac I^Q: Lac repressor gene
lacZ: Beta-galactosidase alpha fragment
rrnBt: E. coli rrnB transcription terminator

FIG. 14



$P_{\phi 10}$: Bacteriophage T7 ϕ10 promoter RBS: Ribosome binding site
Tϕ: T7 ϕ Terminator

FIG. 15

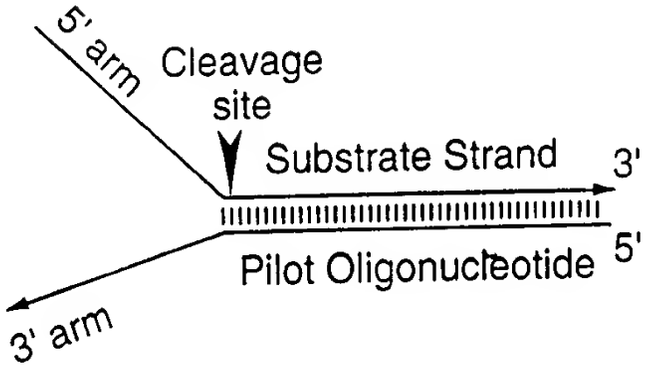


FIG. 16A

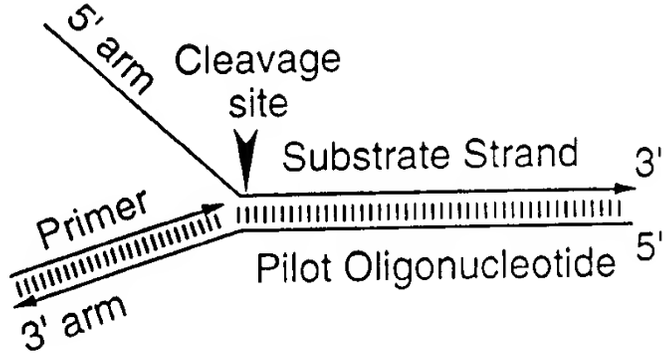


FIG. 16B

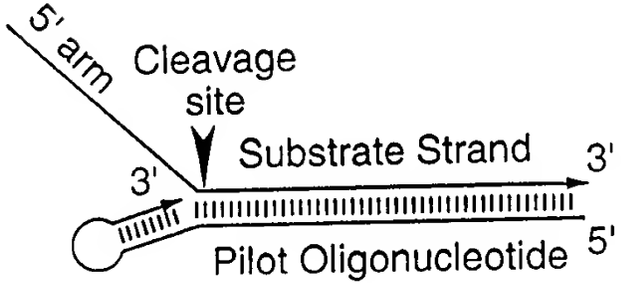


FIG. 16C

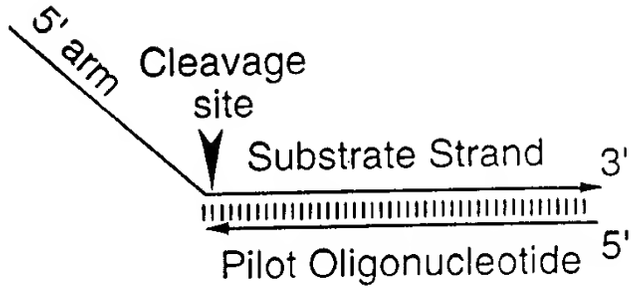


FIG. 16D

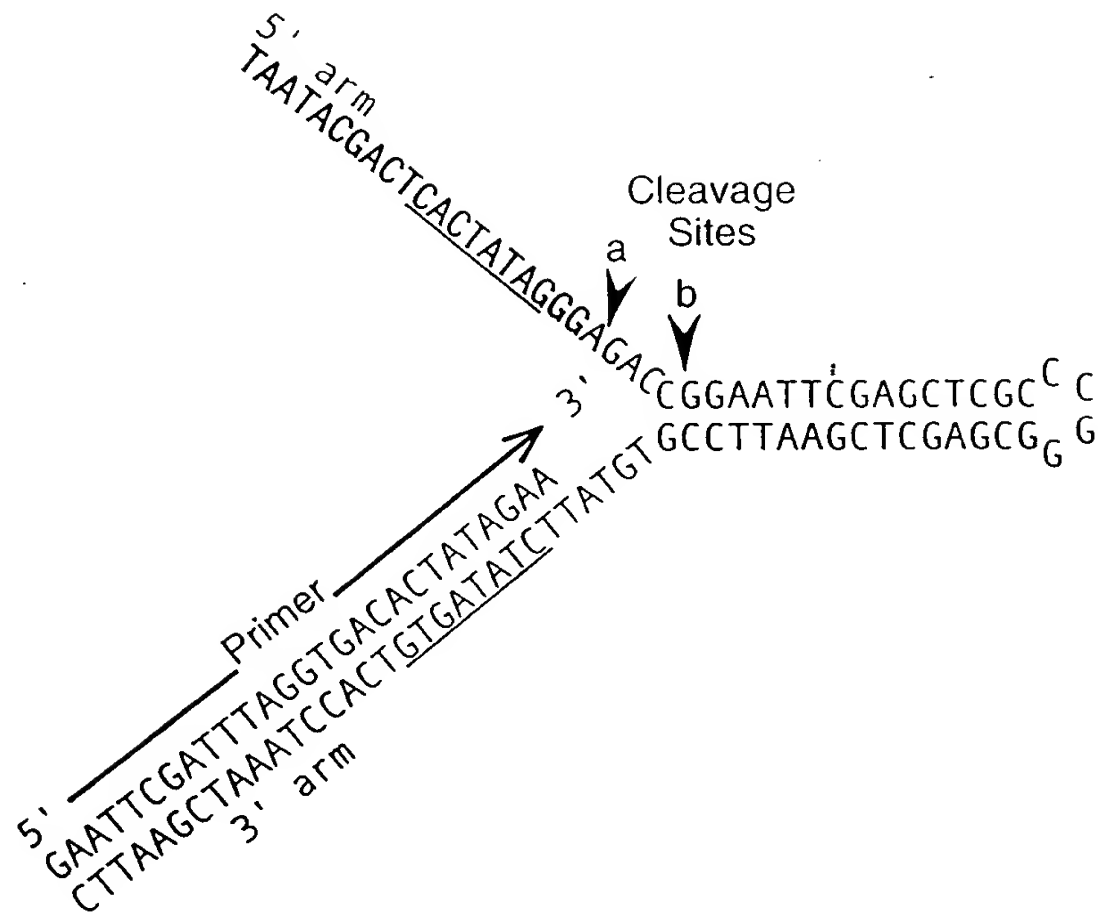

5' arm
TAATACGACTCACTATAGGGAGACCGGAATTCGAGCTCGCC C
Cleavage Sites
a
b
3'
GCCTTAAGCTCGAGCGG G
Primer
5' GAATTCGATTTAGGTGACACTATAGAA
CTTAAGCTAAATCCACTGTGATATCTTATGT
3' arm

FIG. 16E

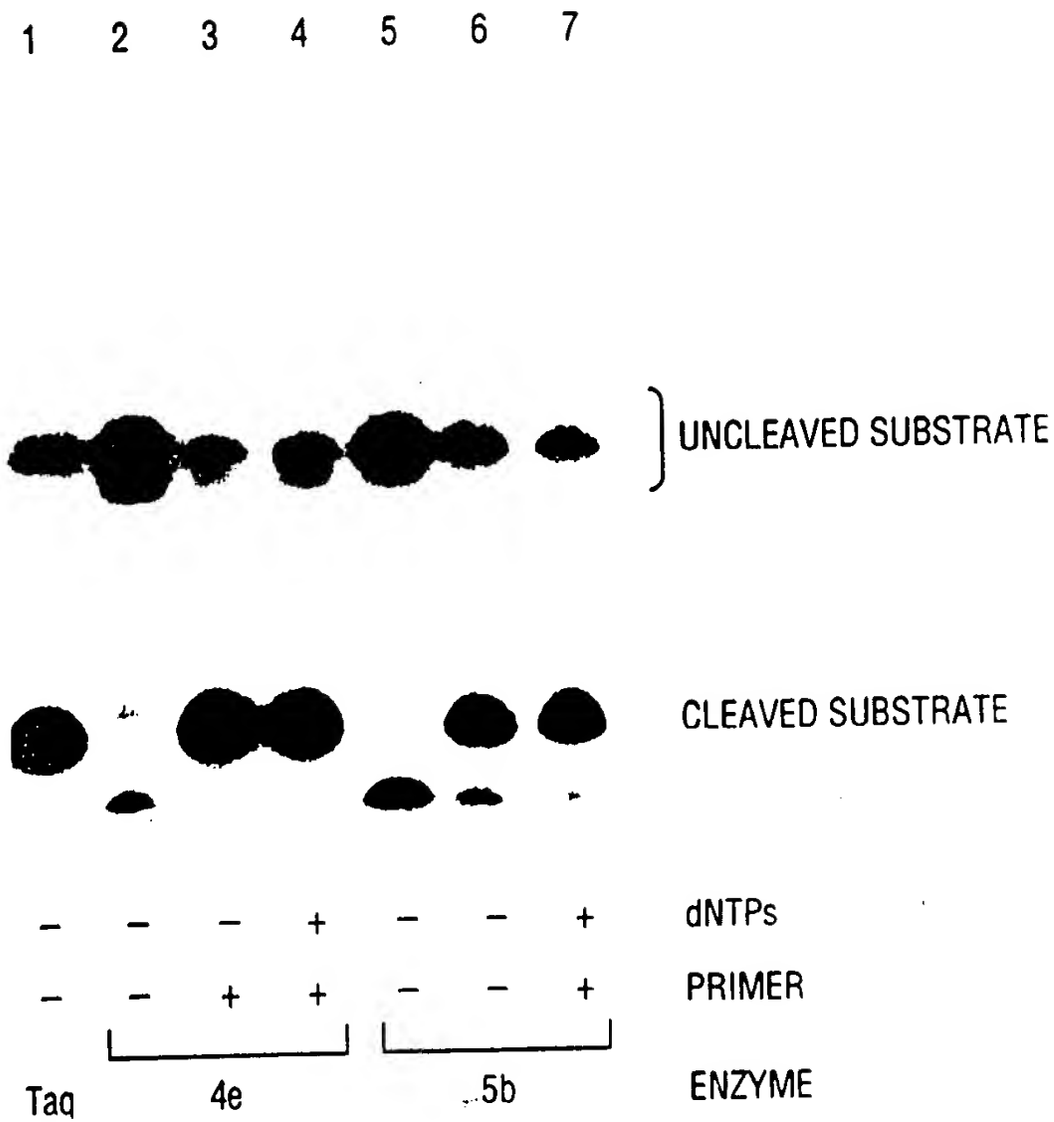


FIG. 17

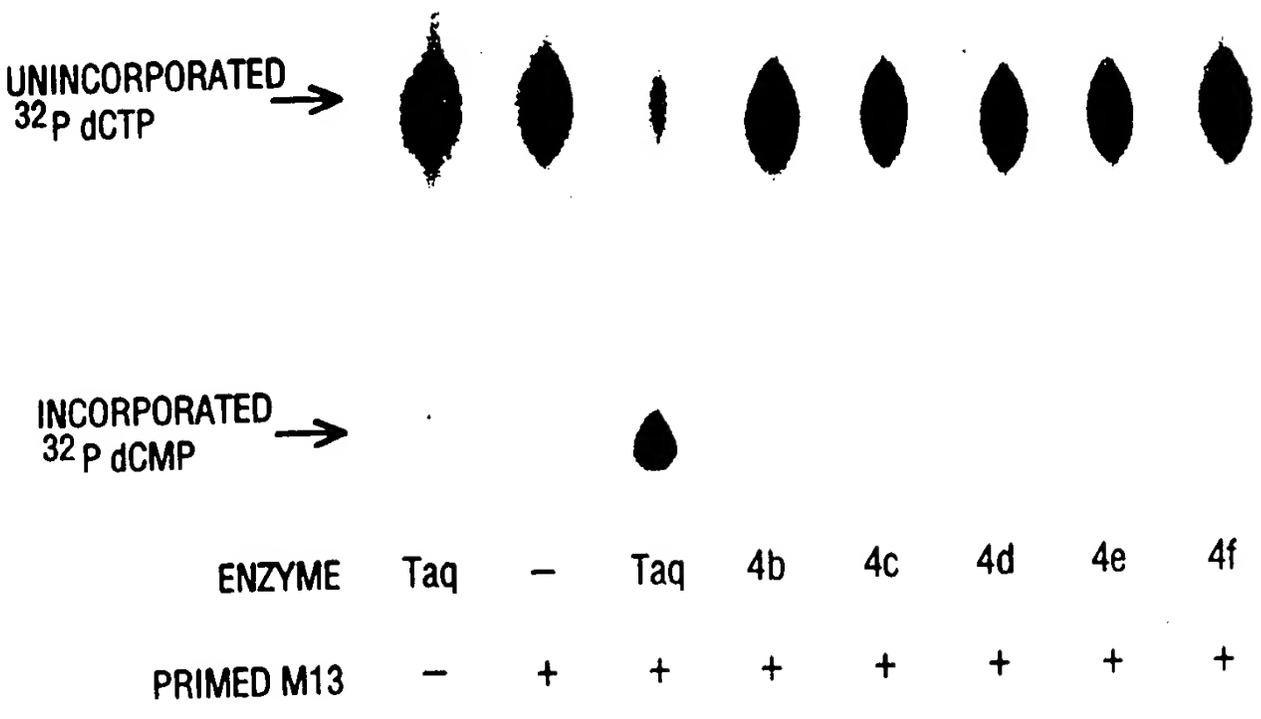

UNINCORPORATED
32P dCTP
INCORPORATED
32P dCMP
ENZYME Taq – Taq 4b 4c 4d 4e 4f
PRIMED M13 – + + + + + + +

FIG. 18

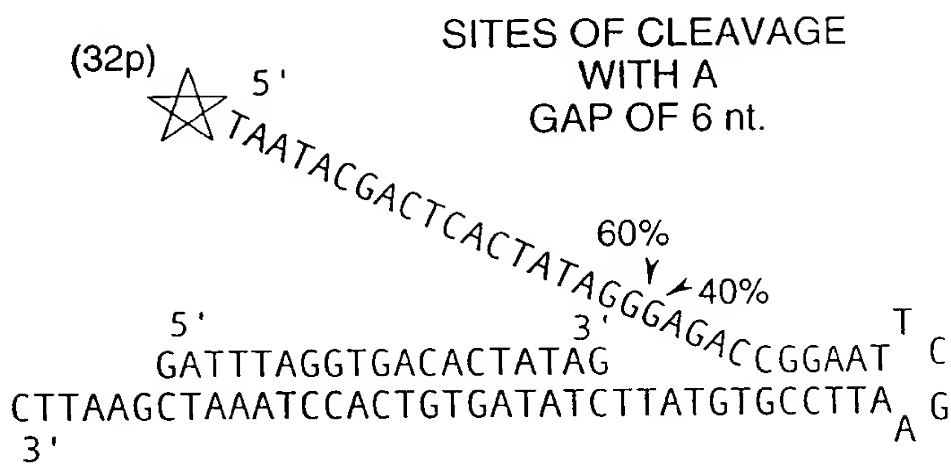


FIG. 19A

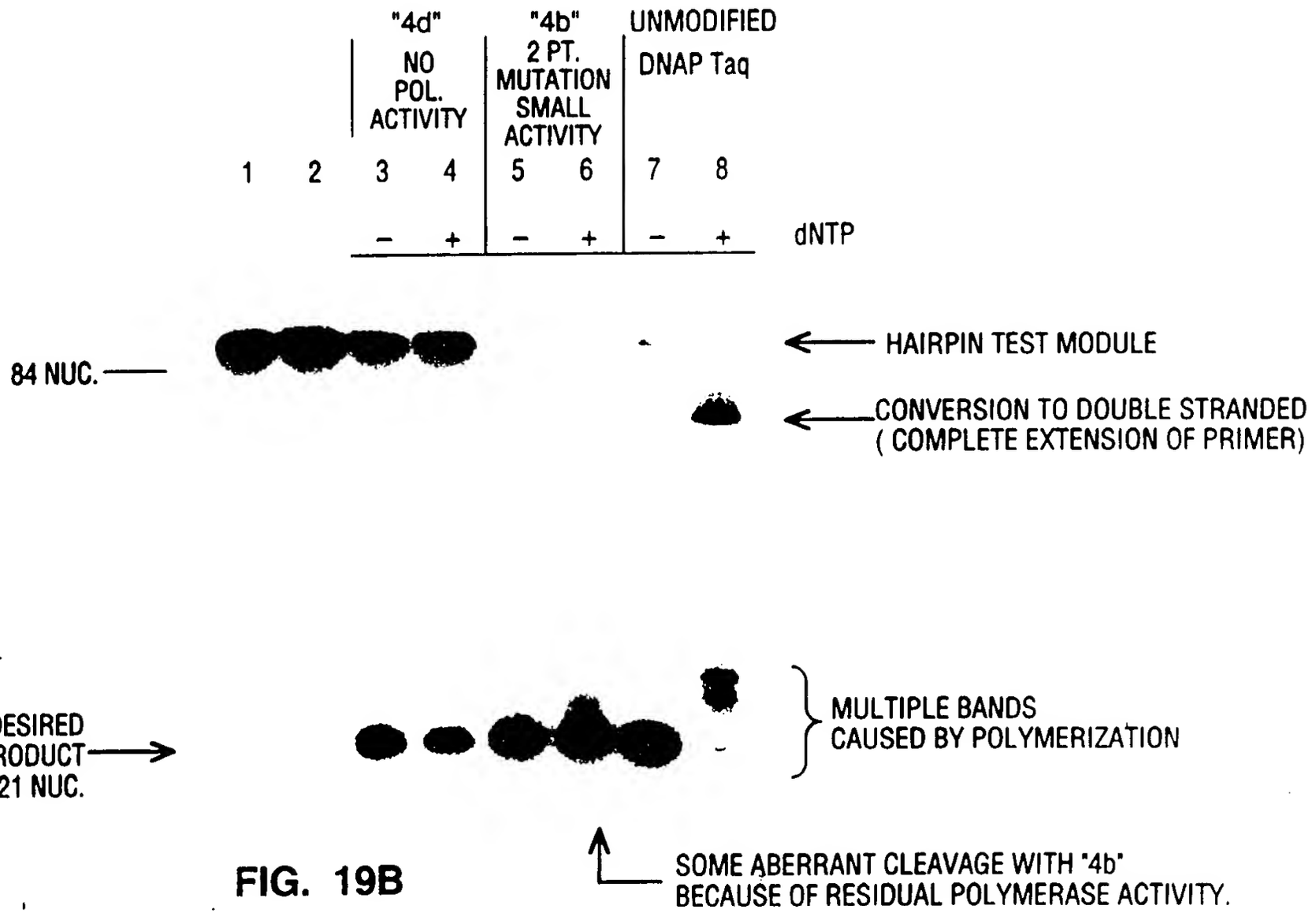

"4d"
NO POL. ACTIVITY
"4b"
2 PT. MUTATION SMALL ACTIVITY
UNMODIFIED
DNAP Taq
1 2 3 4 5 6 7 8
– + – + – +
dNTP
84 NUC.
HAIRPIN TEST MODULE
CONVERSION TO DOUBLE STRANDED
(COMPLETE EXTENSION OF PRIMER)
DESIRED PRODUCT 21 NUC.
MULTIPLE BANDS CAUSED BY POLYMERIZATION
SOME ABERRANT CLEAVAGE WITH "4b" BECAUSE OF RESIDUAL POLYMERASE ACTIVITY.

FIG. 19B

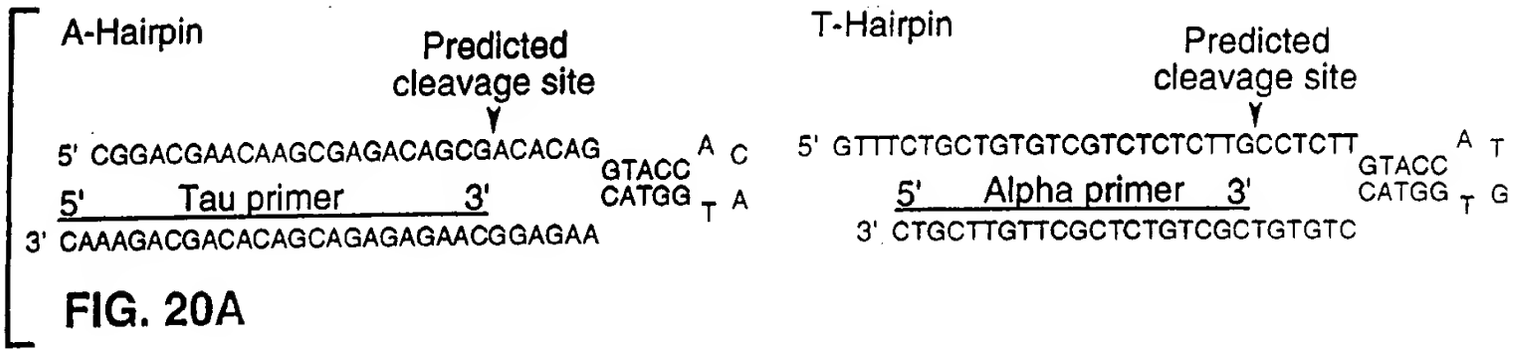


FIG. 20A

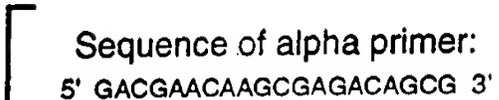


FIG. 20B

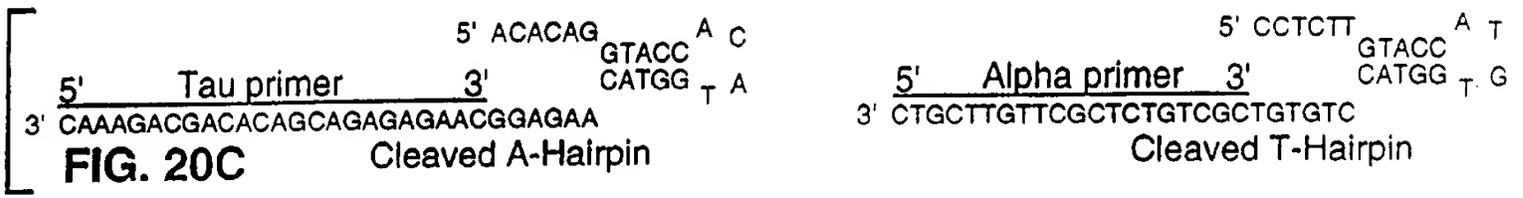


FIG. 20C

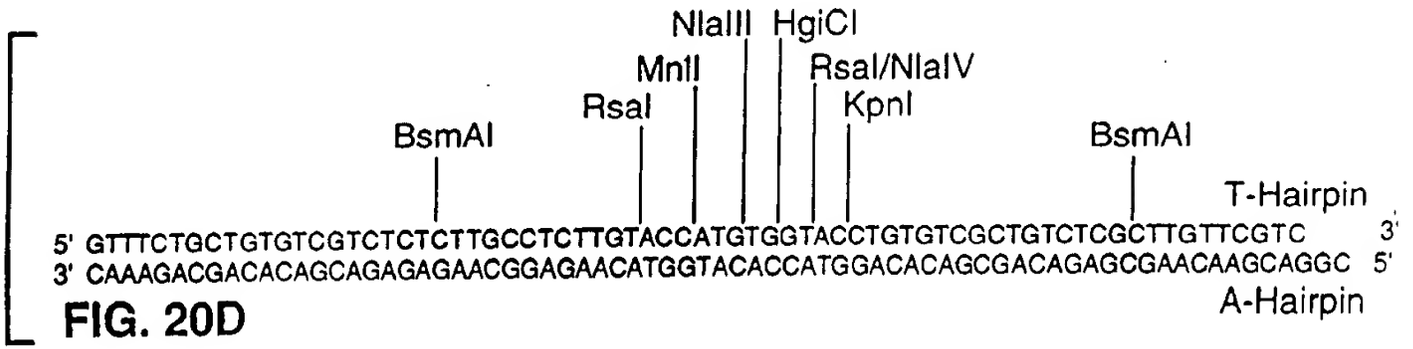


FIG. 20D

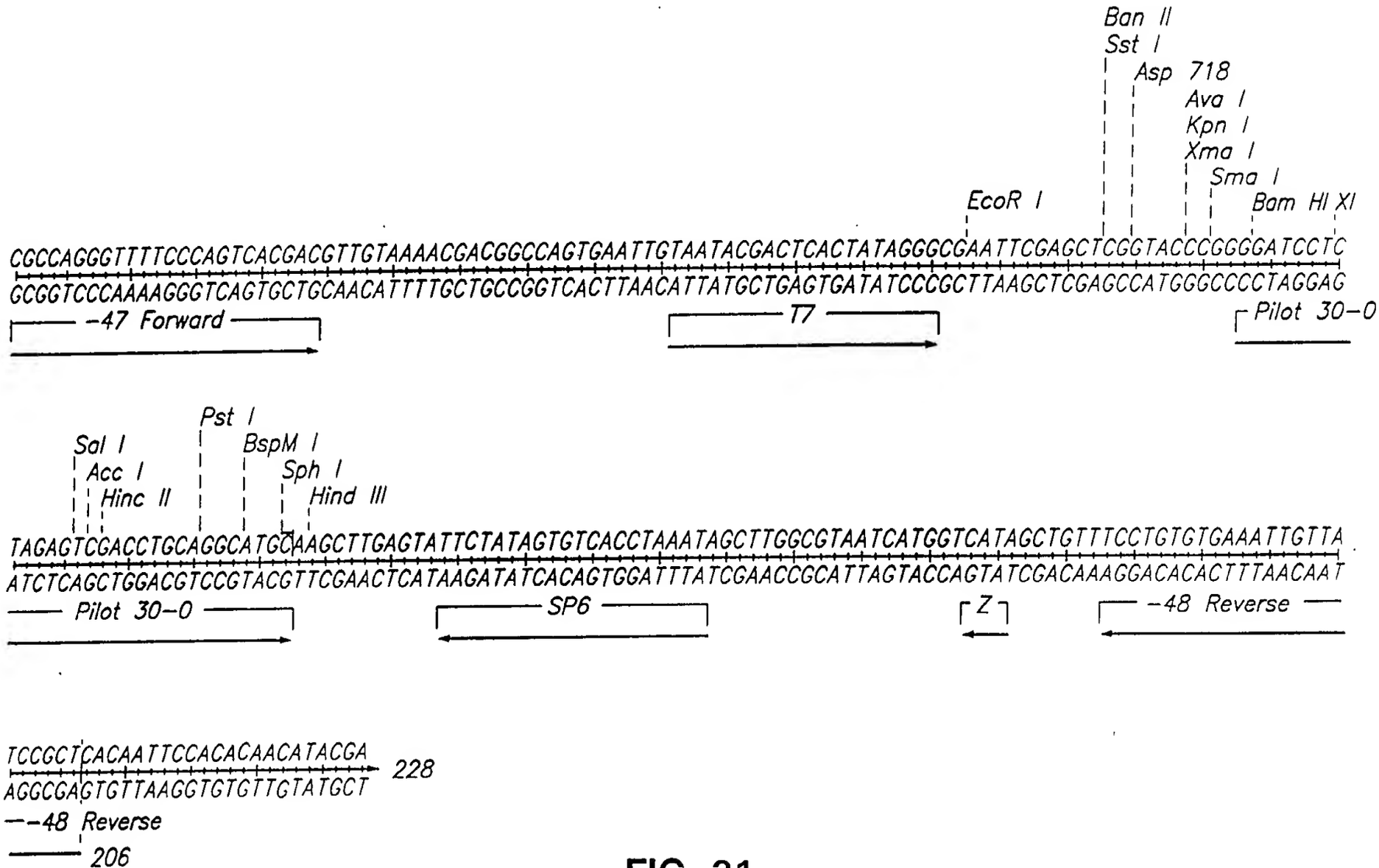

Ban II
Sst I
Asp 718
Ava I
Kpn I
Xma I
Sma I
EcoR I
Bam HI XI
CGCCAGGGTTTTCCCAGTCACGACGTTGTAAAACGACGGCCAGTGAATTGTAATACGACTCACTATAGGGCGAATTCGAGCTCGGTACCCGGGGATCCTC
GCGGTCCCAAAAGGGTCAGTGCTGCAACATTTTGCTGCCGGTCACTTAACATTATGCTGAGTGATATCCCGCTTAAGCTCGAGCCATGGGCCCCTAGGAG
-47 Forward
T7
Pilot 30-0
Pst I
Sal I
BspM I
Acc I
Sph I
Hinc II
Hind III
TAGAGTCGACCTGCAGGCATGCAAGCTTGAGTATTCTATAGTGTCACCTAAATAGCTTGGCGTAATCATGGTCATAGCTGTTTCCTGTGTGAAATTGTTA
ATCTCAGCTGGACGTCCGTACGTTCGAACTCATAAGATATCACAGTGGATTTATCGAACCGCATTAGTACCAGTATCGACAAAGGACACACTTTAACAAT
Pilot 30-0
SP6
Z
-48 Reverse
TCCGCTCACAATTCCACACAACATACGA
AGGCGAGTGTTAAGGTGTGTTGTATGCT
228
-48 Reverse
206

FIG. 21

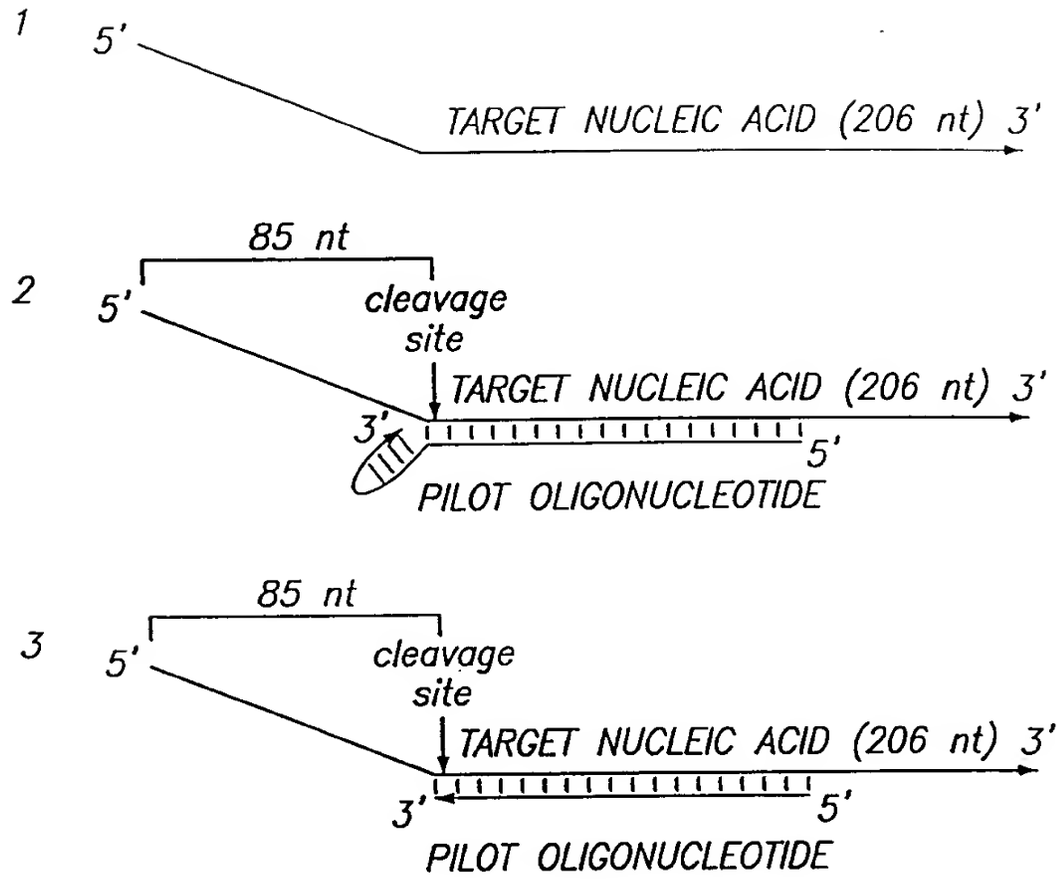


FIG. 22A

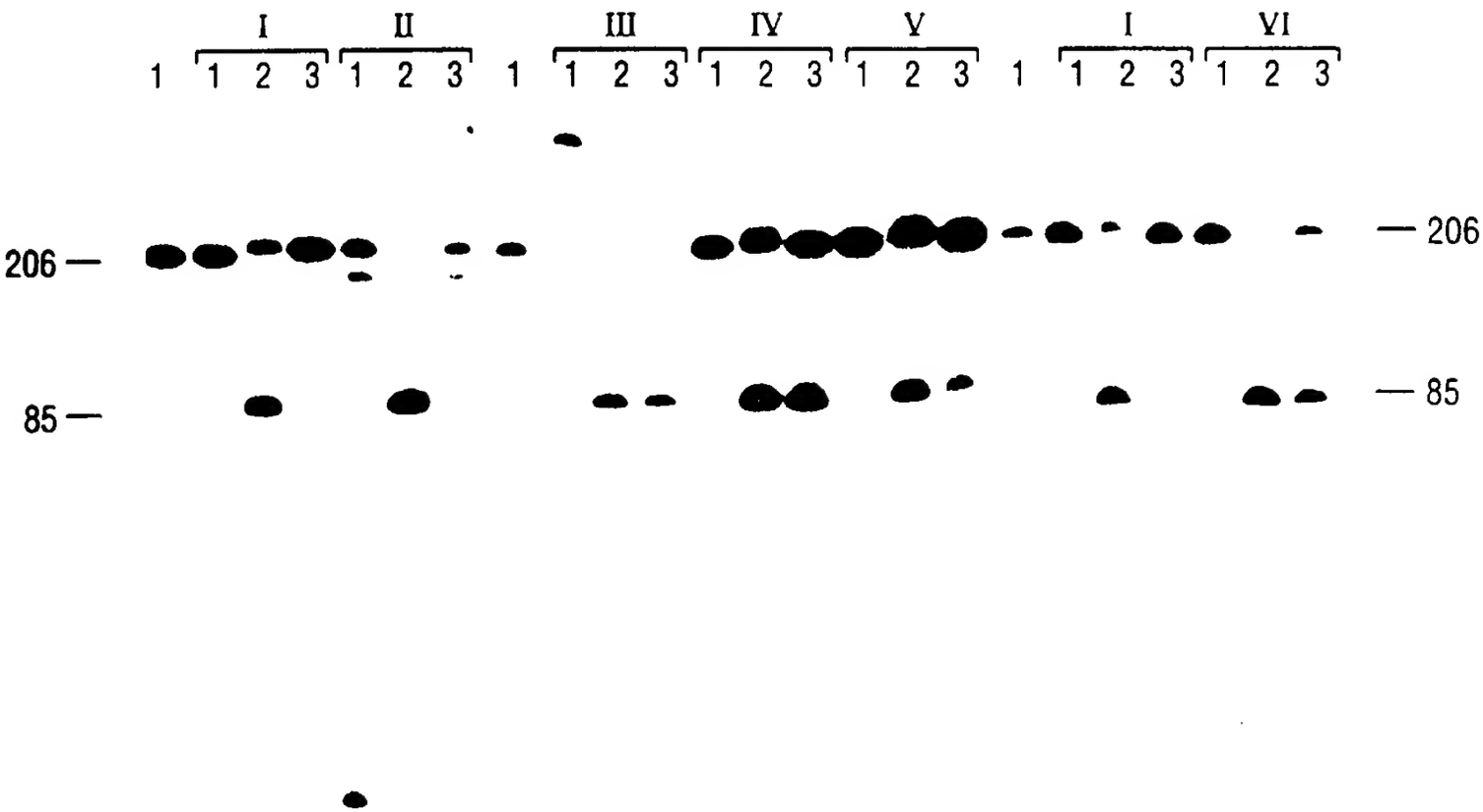


FIG. 22B

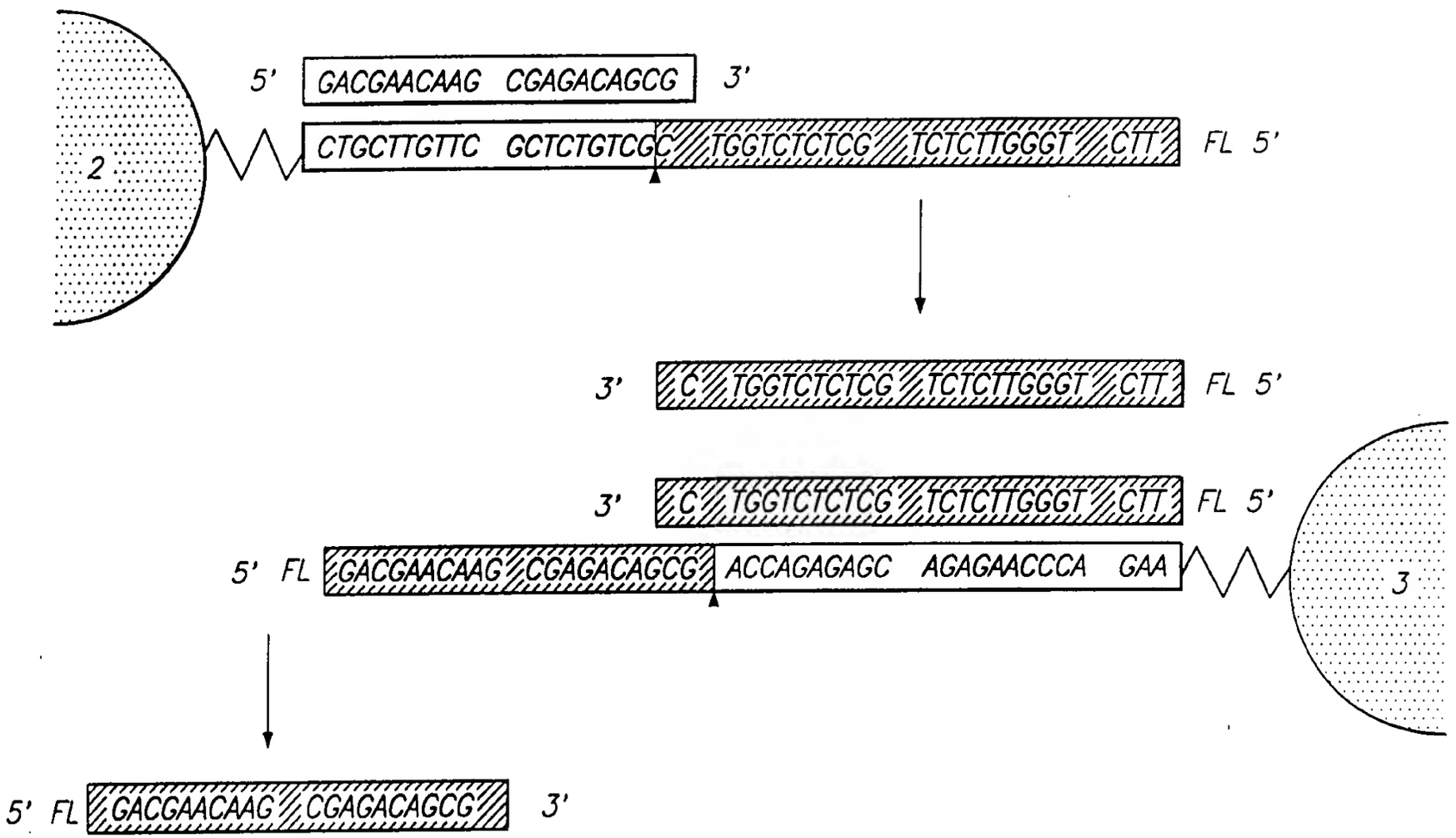

5' GACGAACAAG CGAGACAGCG 3'
CTGCTTGTTC GCTCTGTCGC TGGTCTCTCG TCTCTTGGGT CTT FL 5'
2
3' C TGGTCTCTCG TCTCTTGGGT CTT FL 5'
3' C TGGTCTCTCG TCTCTTGGGT CTT FL 5'
5' FL GACGAACAAG CGAGACAGCG ACCAGAGAGC AGAGAACCCA GAA
3
5' FL GACGAACAAG CGAGACAGCG 3'

FIG. 23

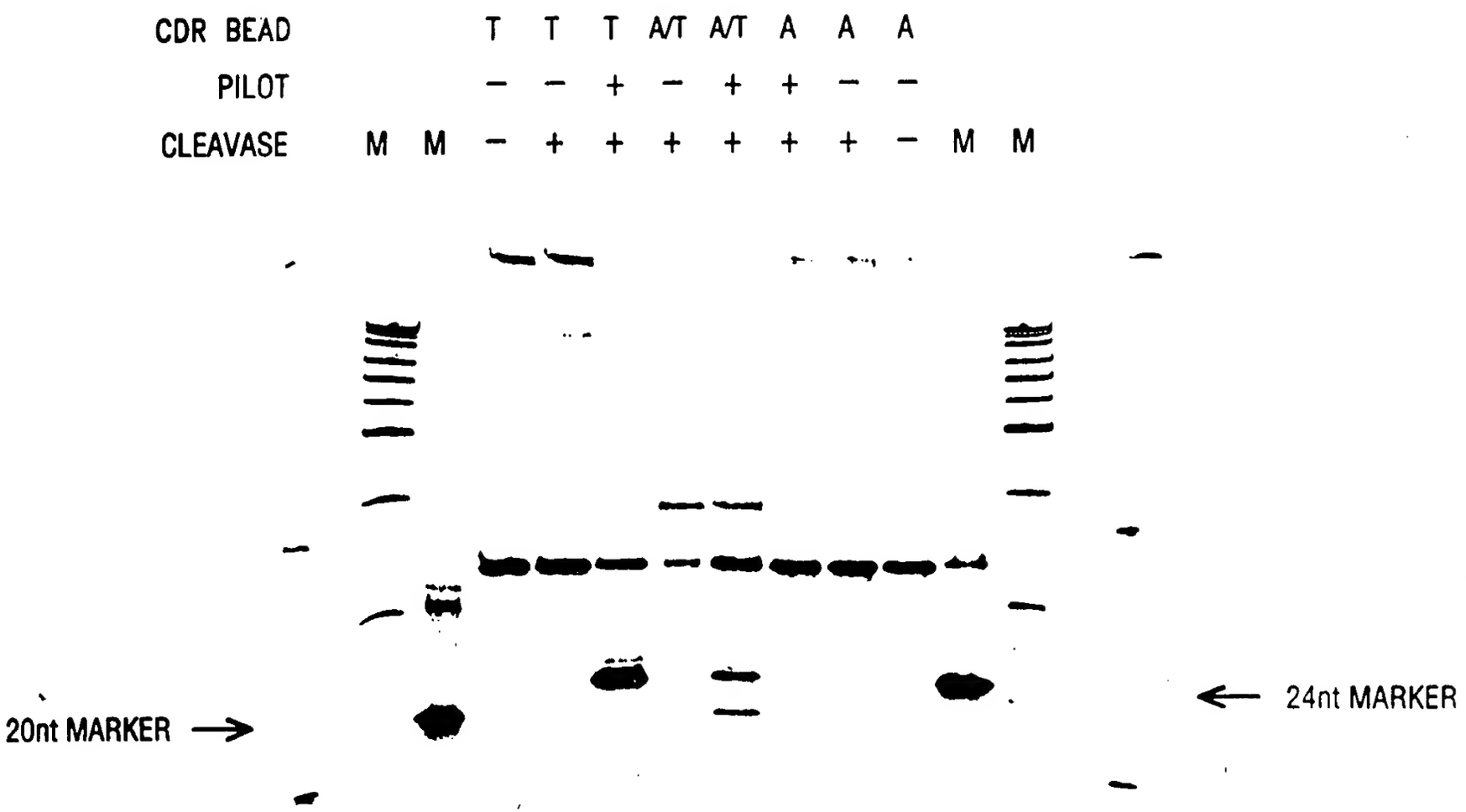

CDR BEAD T T T A/T A/T A A A
PILOT − − + − + + − −
CLEAVASE M M − + + + + + + − M M
20nt MARKER
24nt MARKER

FIG. 24

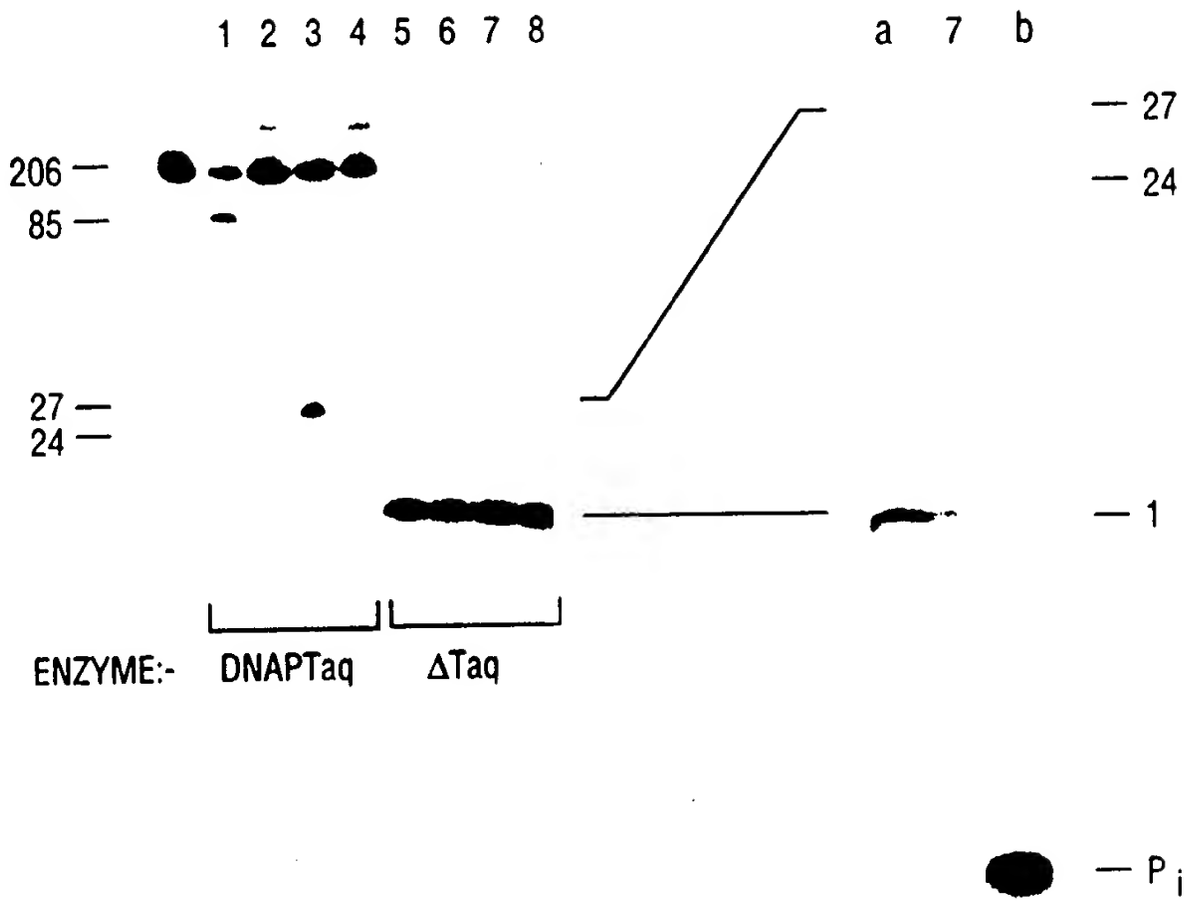


FIG. 25A

FIG. 25B

FIG. 26A

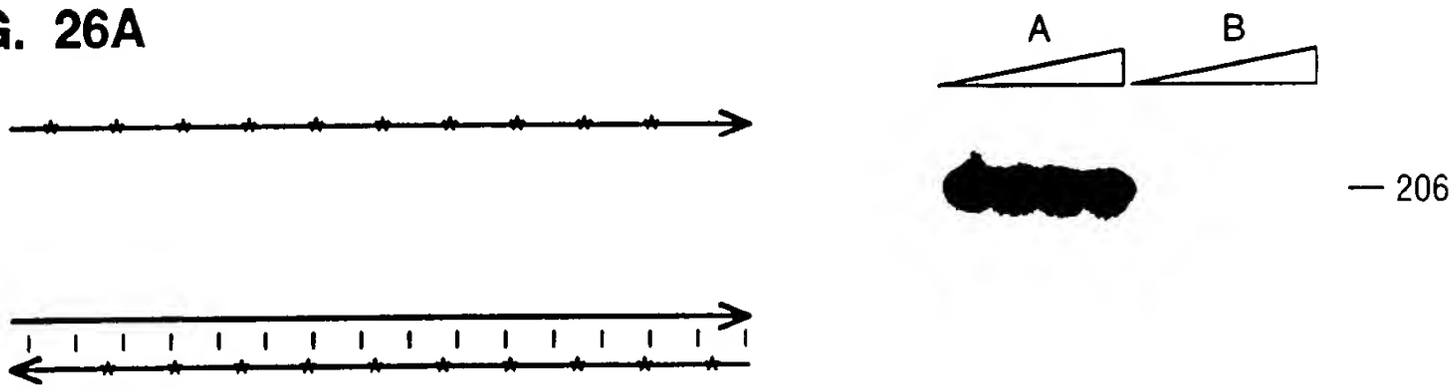


FIG. 26B

* = ^{32}P

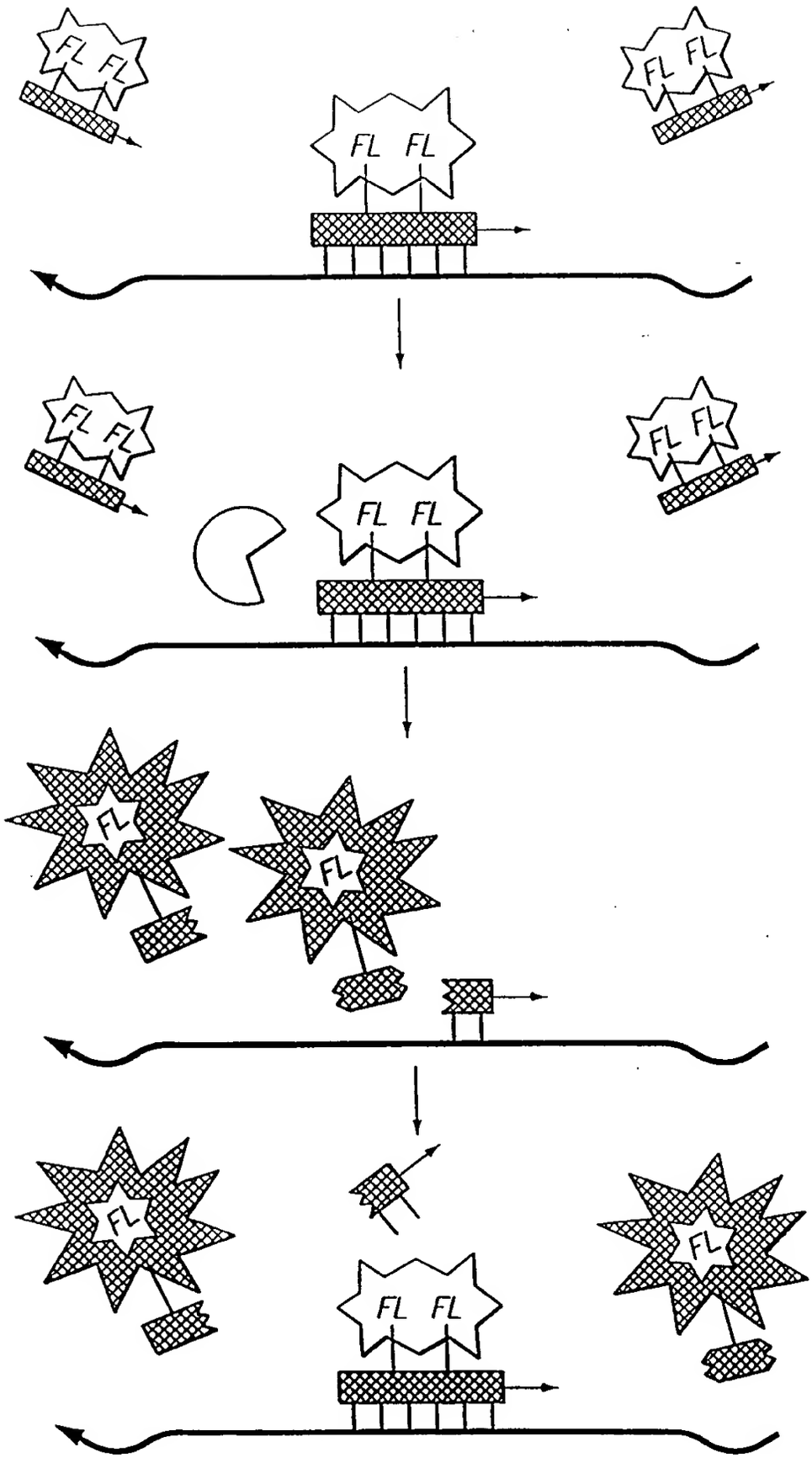


FIG. 27

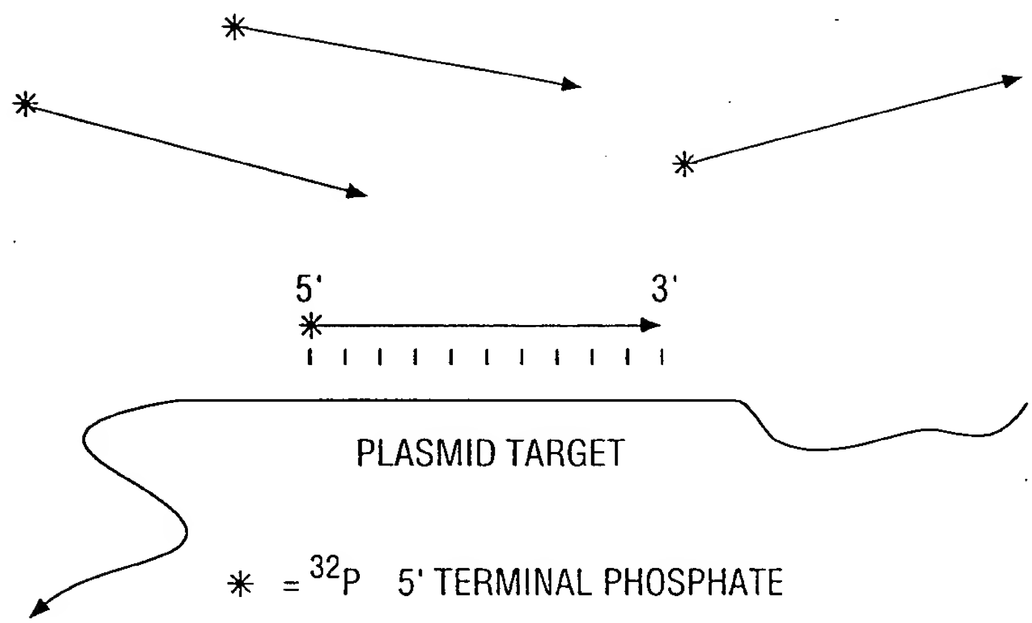


FIG. 28A

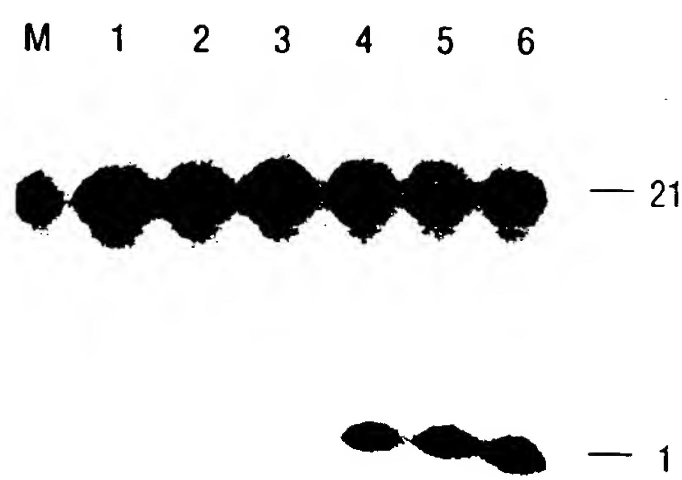


FIG. 28B

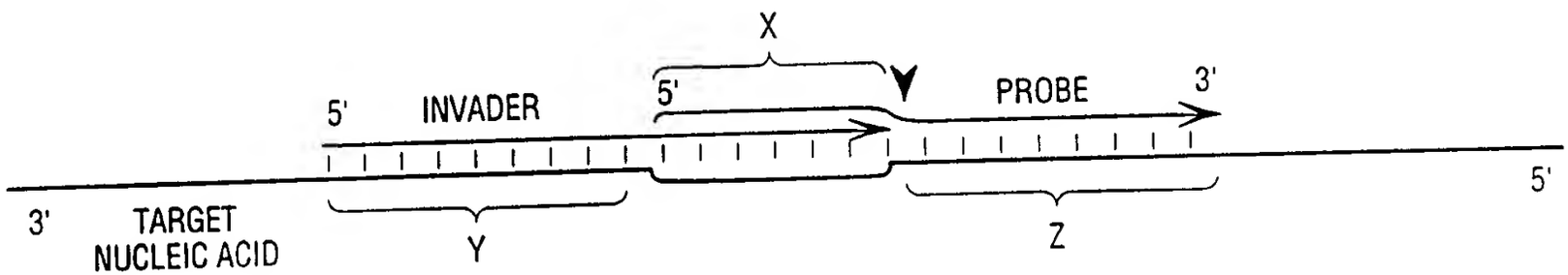


FIG. 29

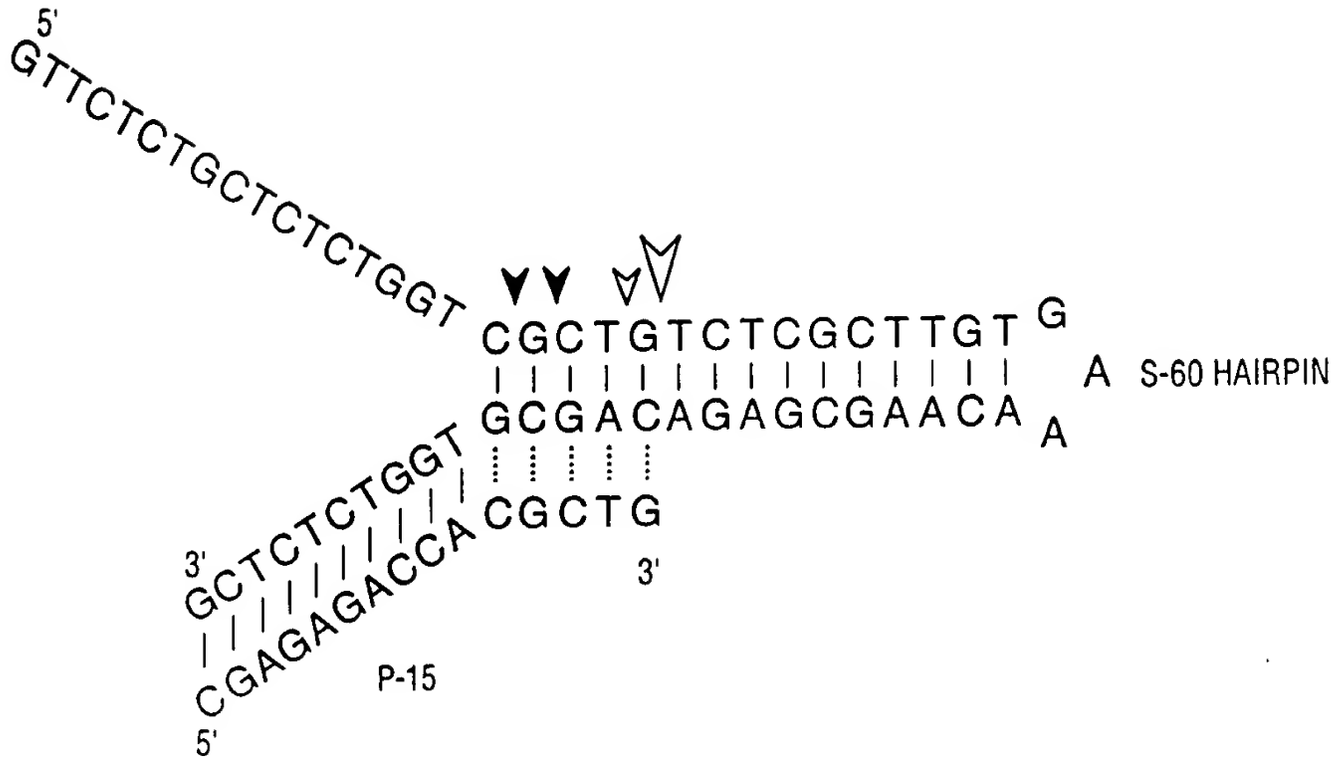

5'
GTTCTCTGCTCTCTGGT
CGCTGTCTCGCTTGT G
A
S-60 HAIRPIN
GCGACAGAGCGAACA A
CGCTG
3'
GCTCTCTGGT
CGAGAGACCA
3'
P-15
5'

FIG. 30

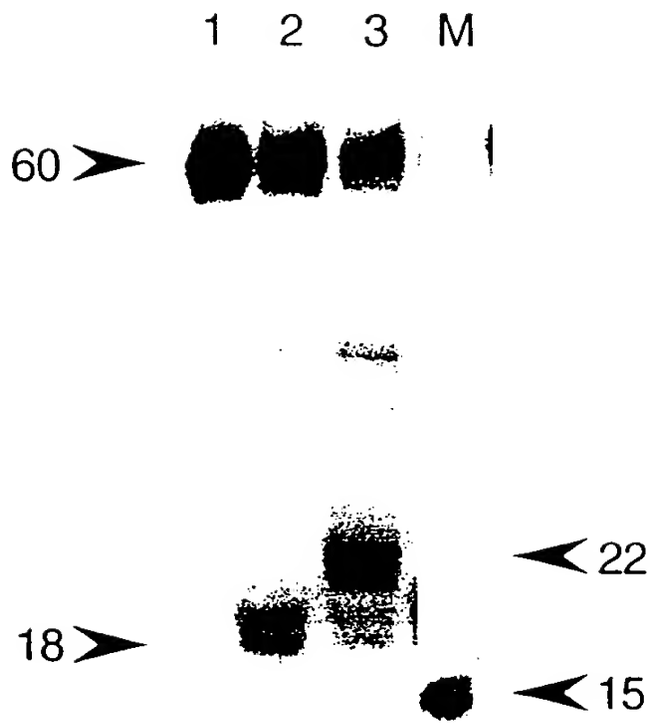


FIG. 31

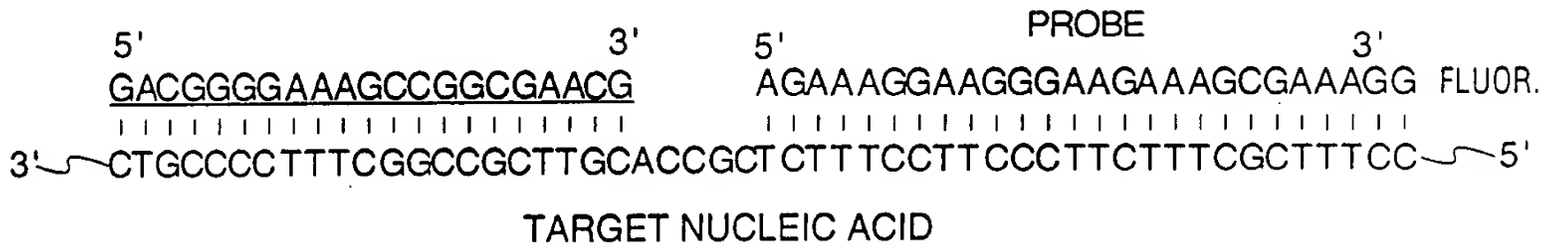


FIG. 32A

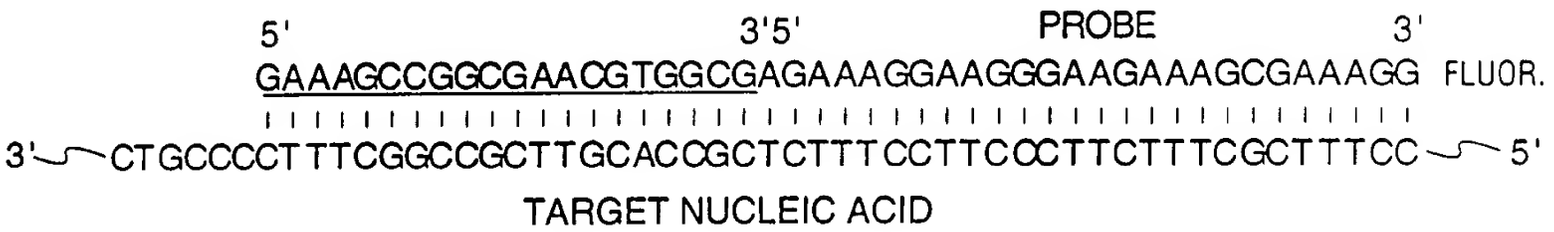


FIG. 32B

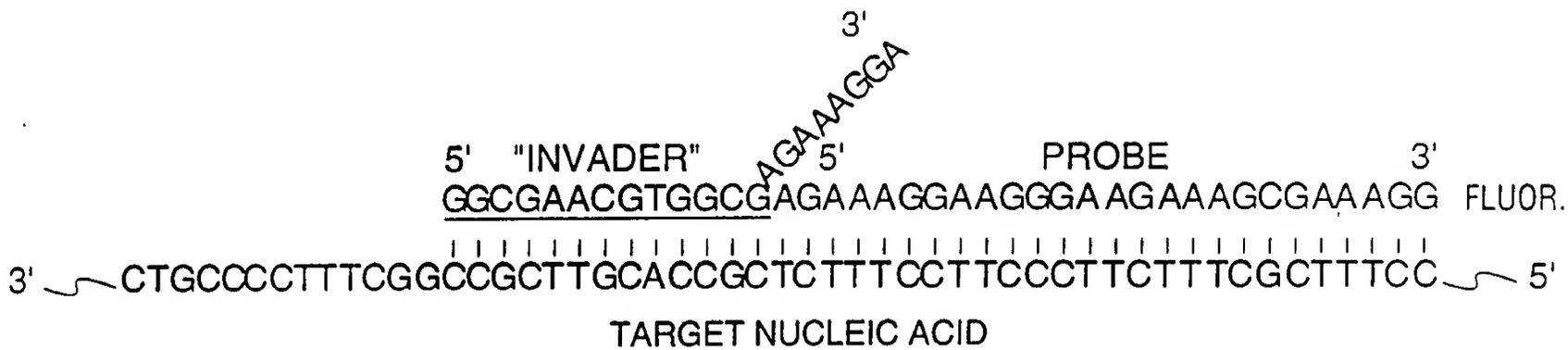


FIG. 32C

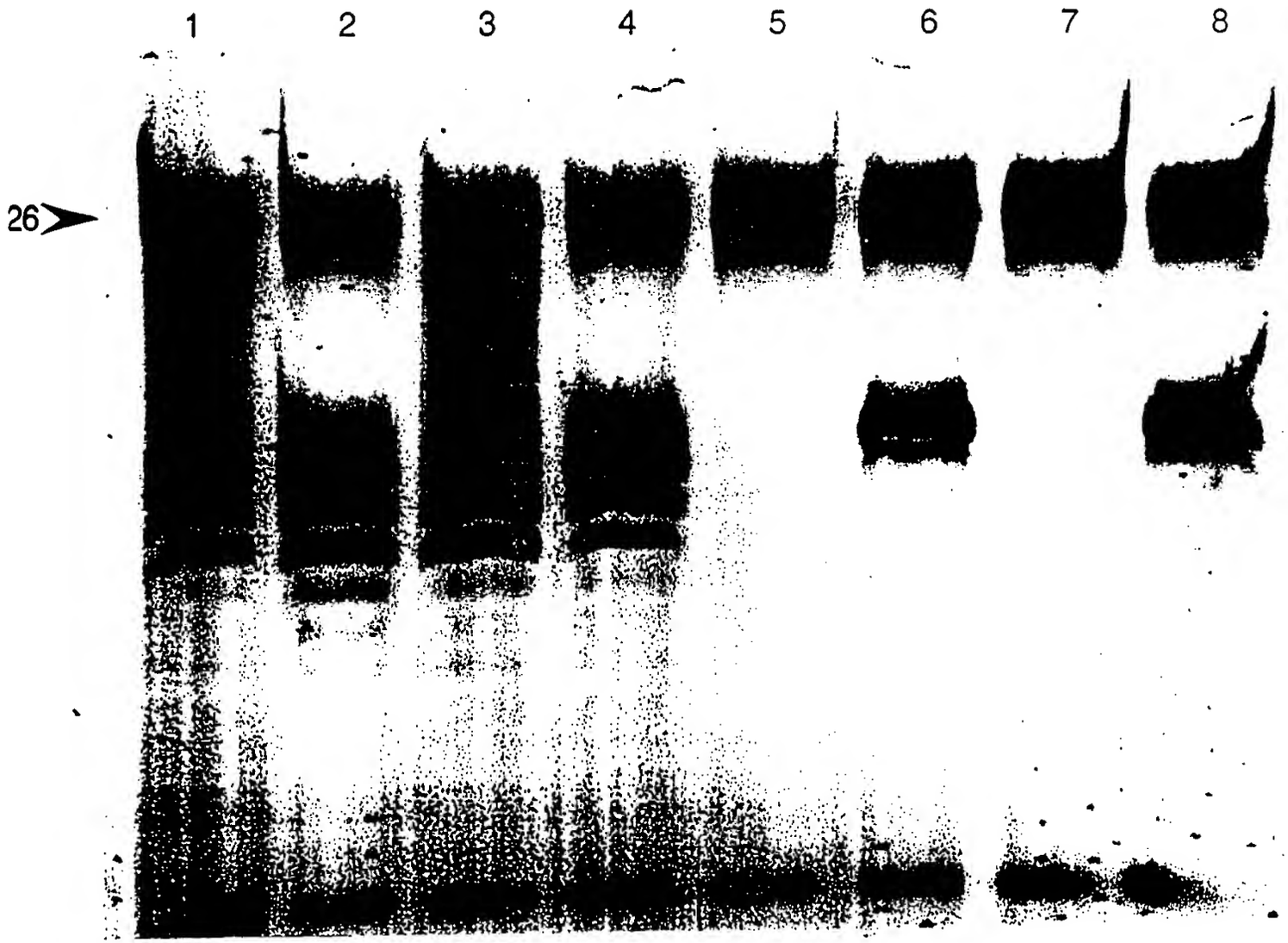


FIG. 33

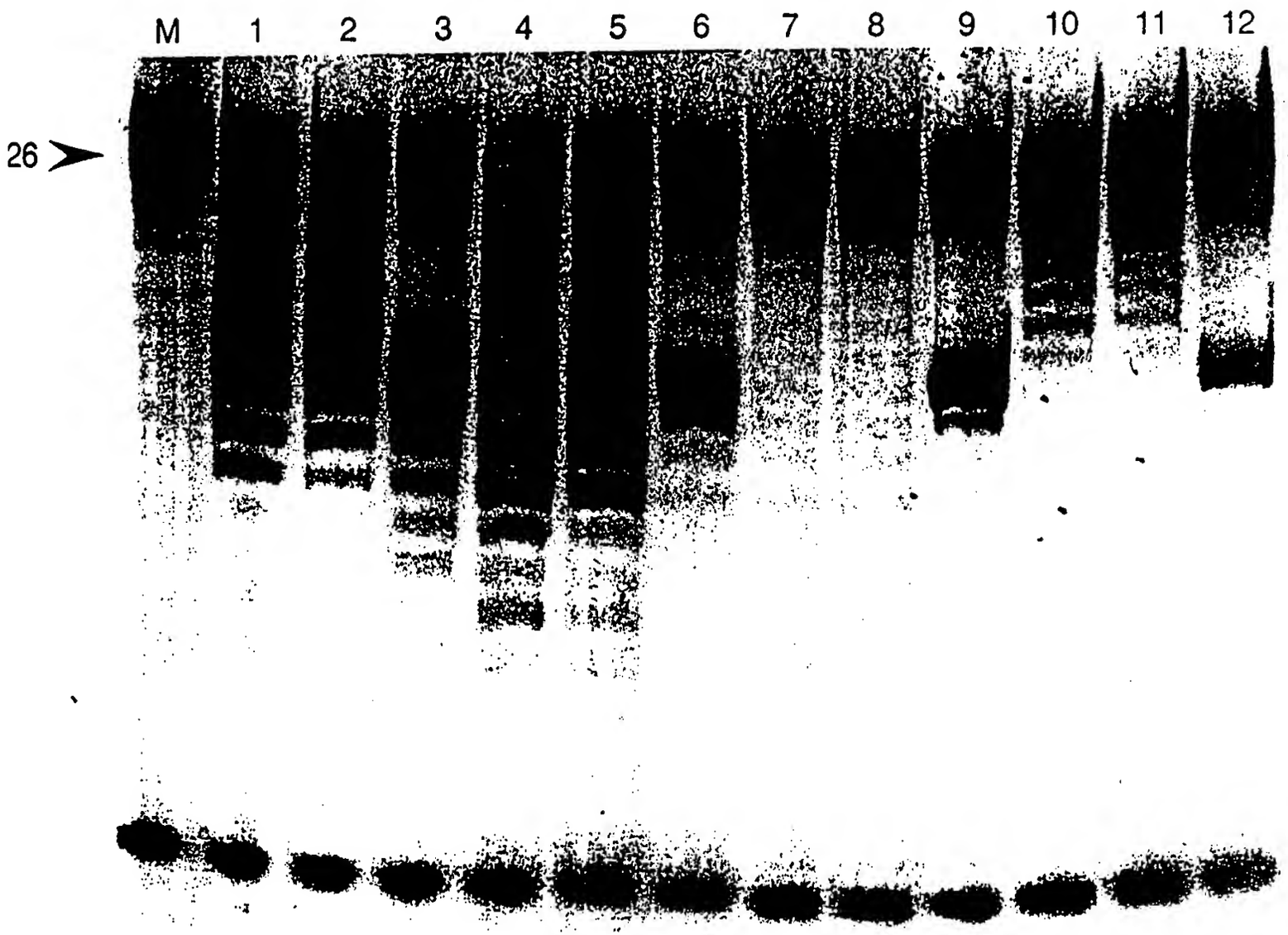


FIG. 34

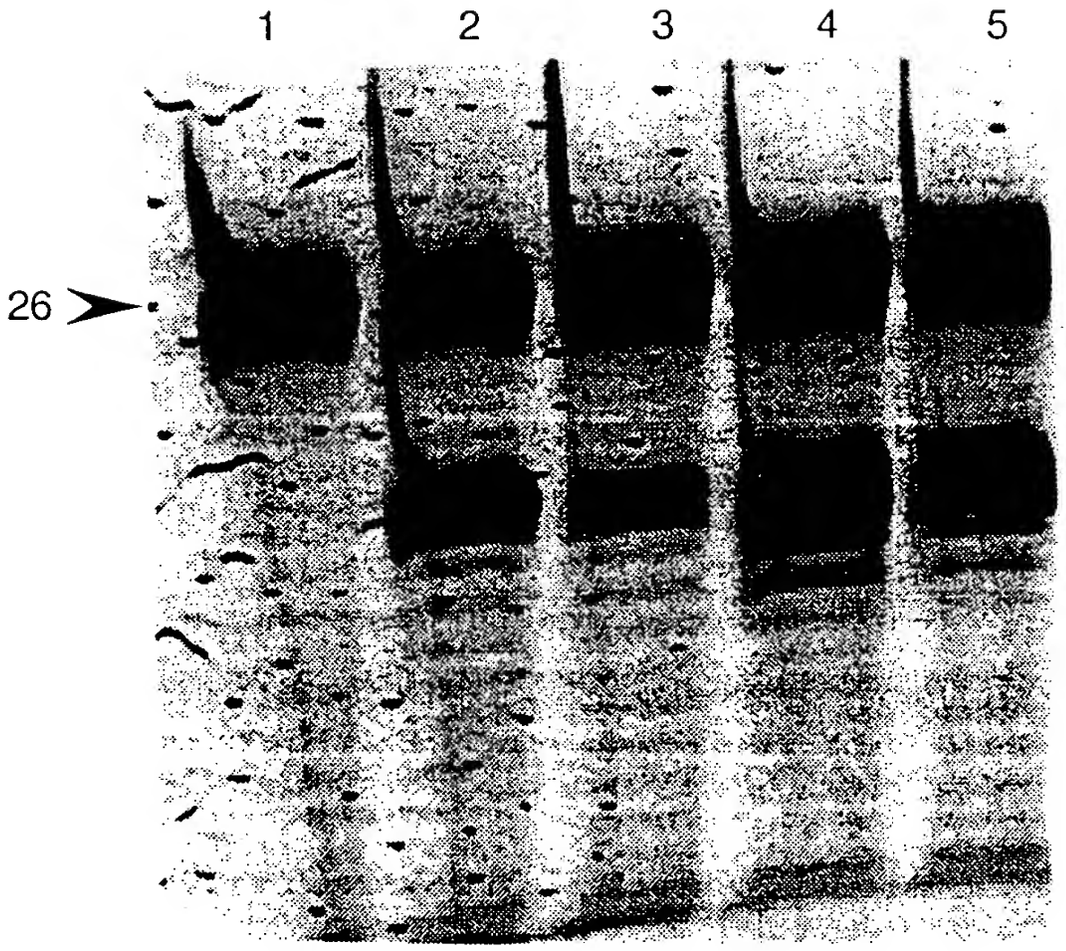


FIG. 35

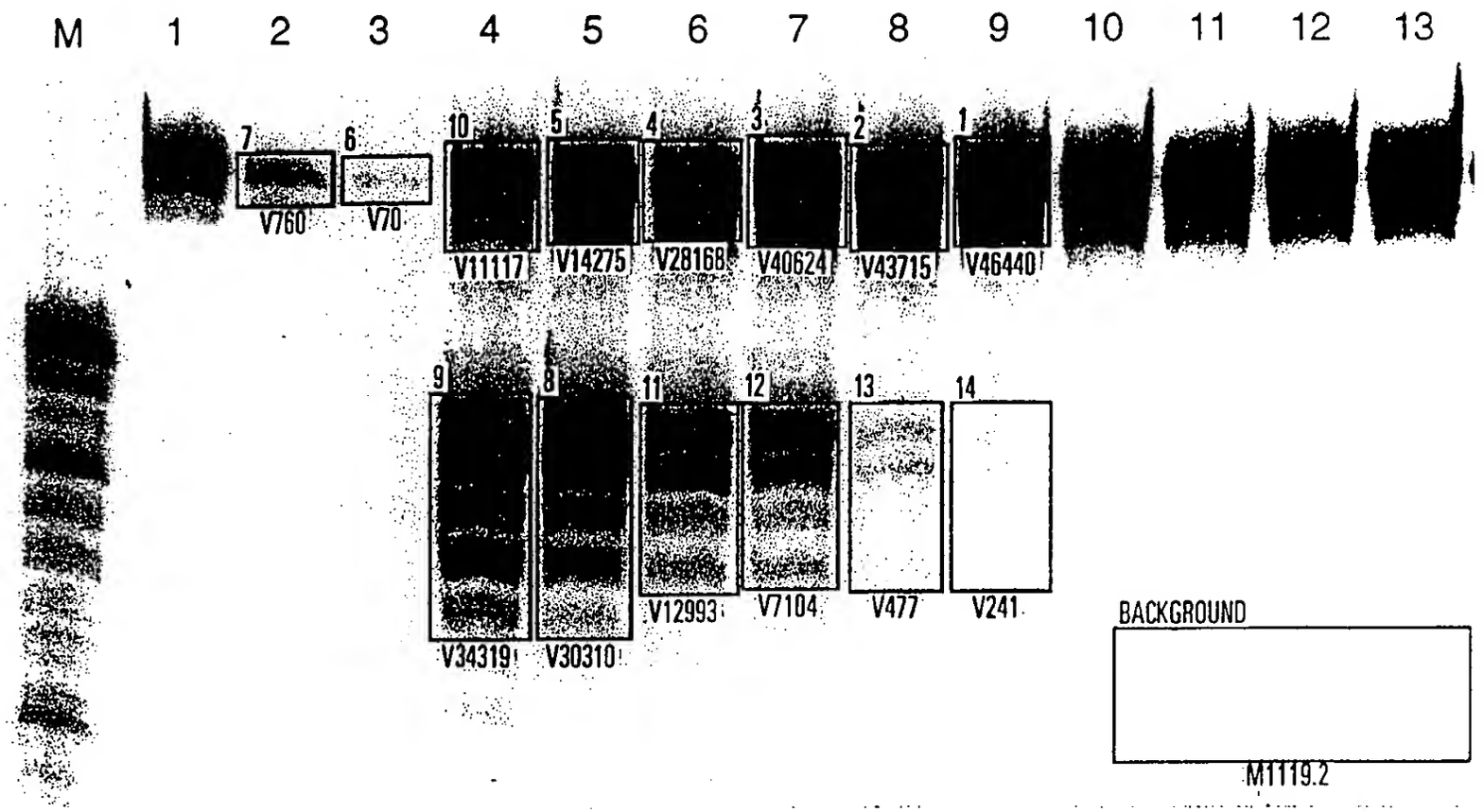

M
1
2
3
4
5
6
7
8
9
10
11
12
13
V760
V70
V11117
V14275
V28168
V40624
V43715
V46440
V34319
V30310
V12993
V7104
V477
V241
BACKGROUND
M1119.2

FIG. 36

FIG. 37

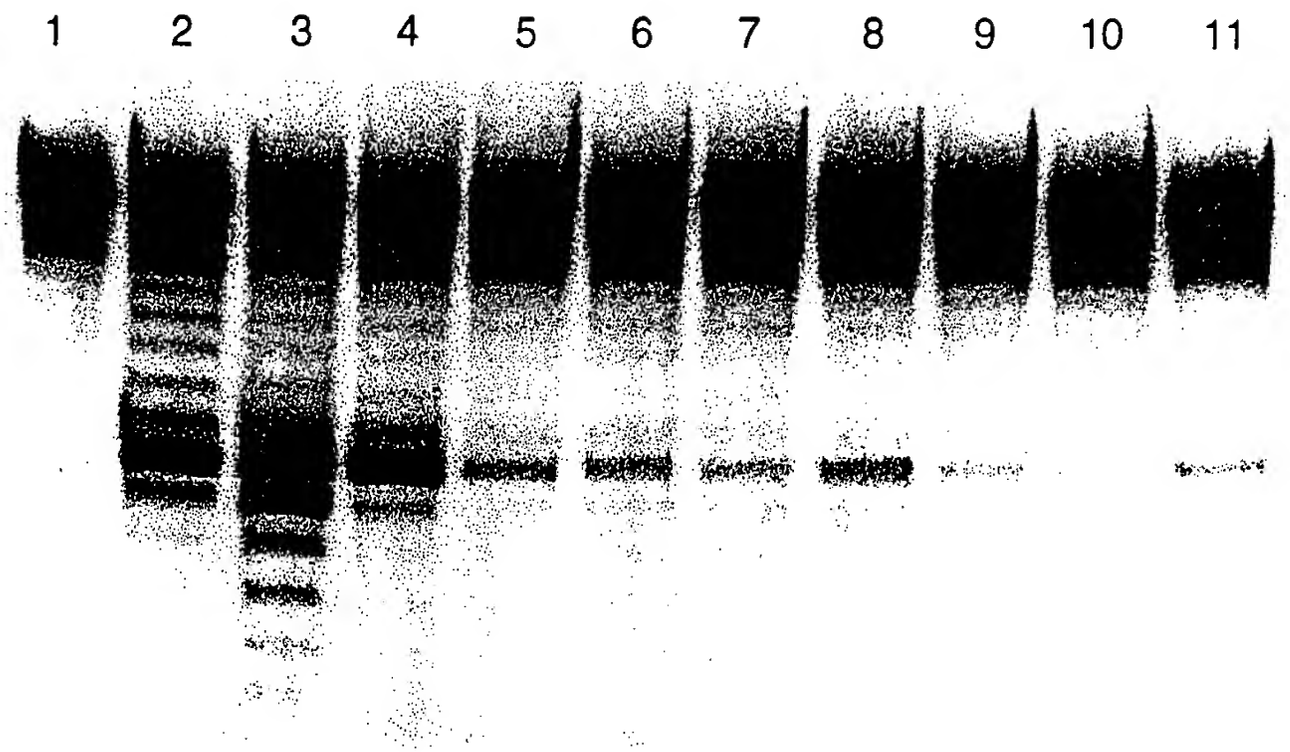


FIG. 38

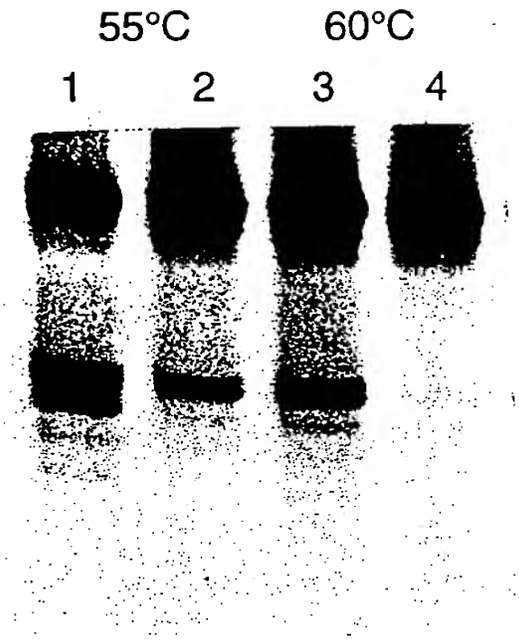


FIG. 39

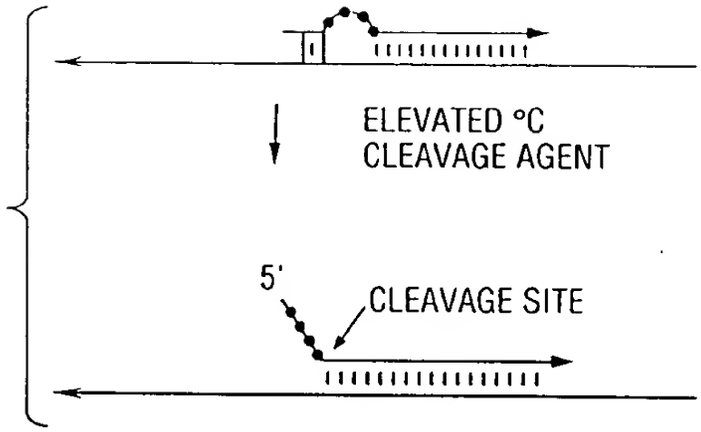


FIG. 40A

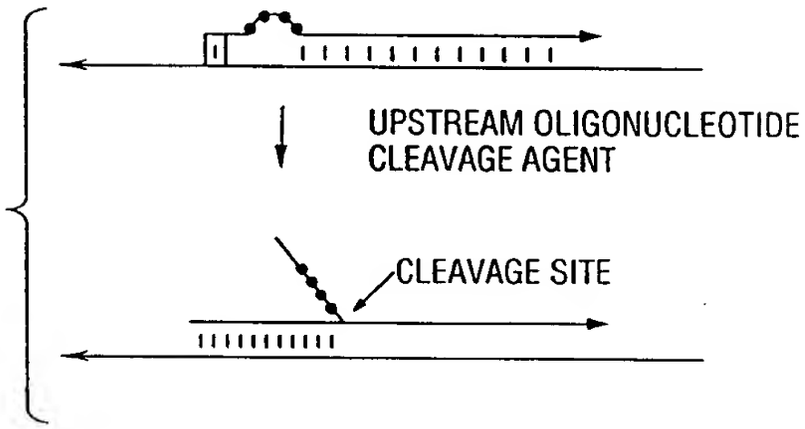


FIG. 40B

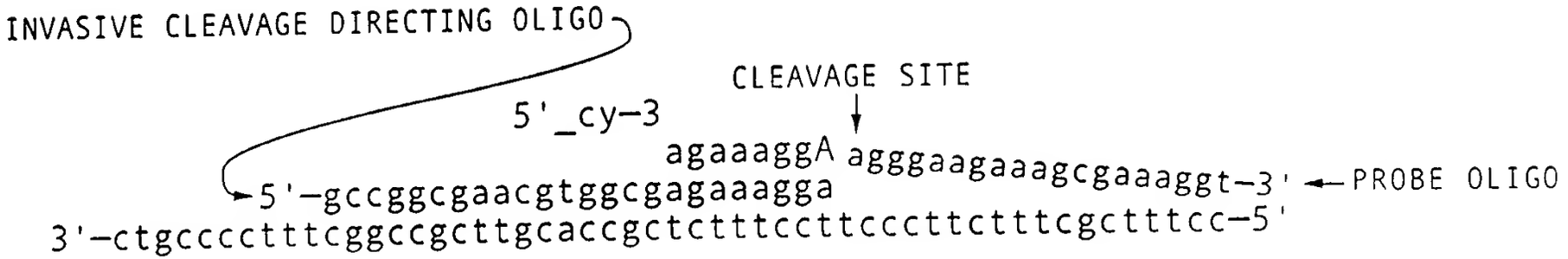

INVASIVE CLEAVAGE DIRECTING OLIGO
CLEAVAGE SITE
5'_cy–3
agaaaggA agggaagaaagcgaaaggt–3' ← PROBE OLIGO
5'–gccggcgaacgtggcgagaaagga
3'–ctgccccttcggccgcttgcaccgctctttccttcccttctttcgctttcc–5'

FIG. 41

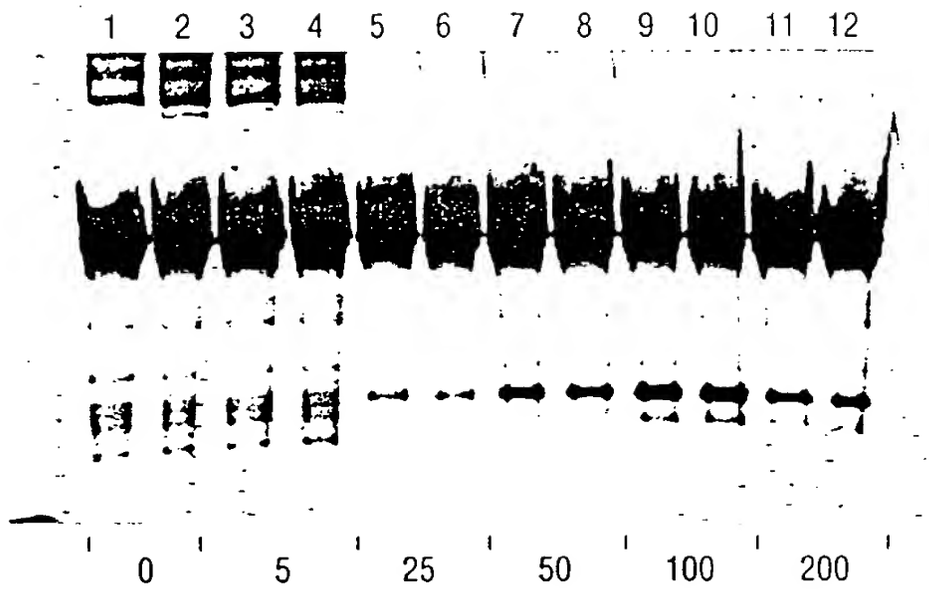


FIG. 42

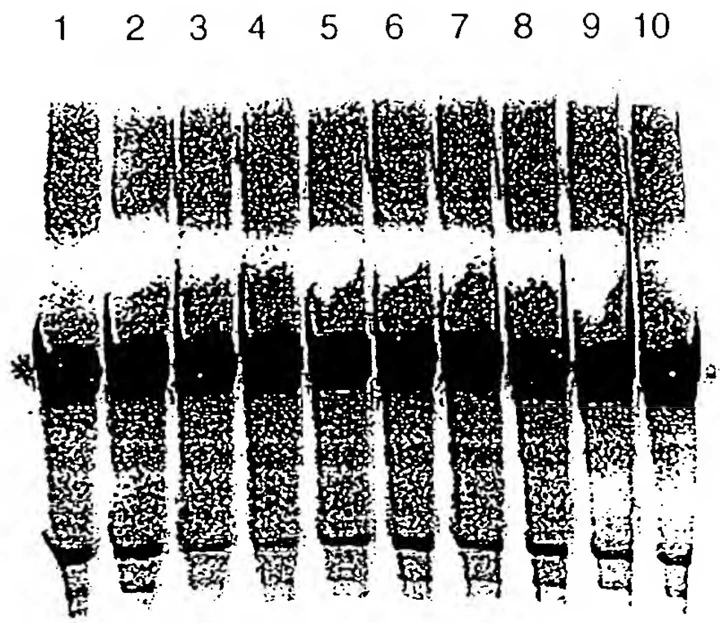


FIG. 43

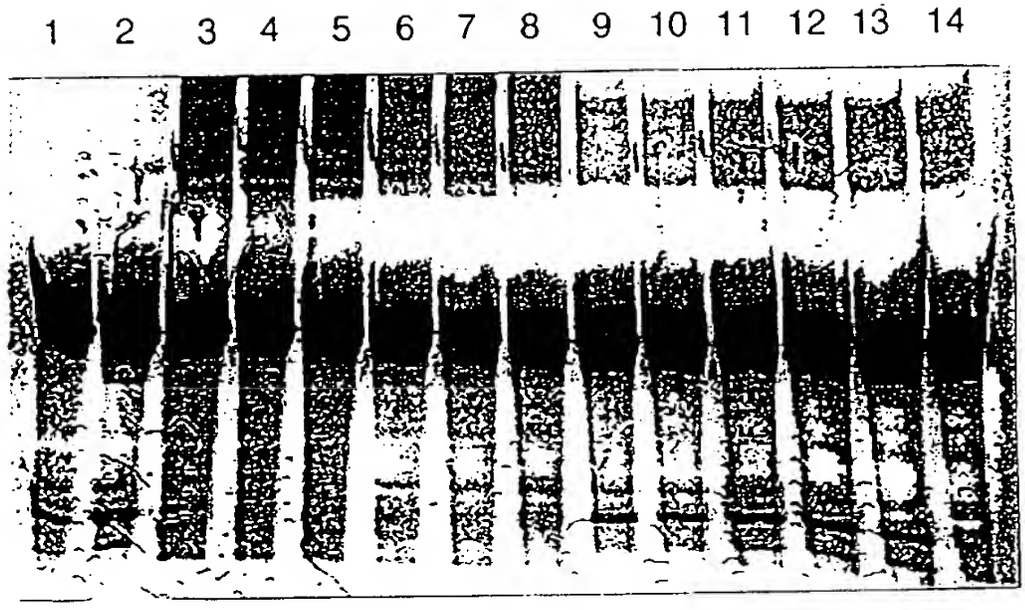


FIG. 44

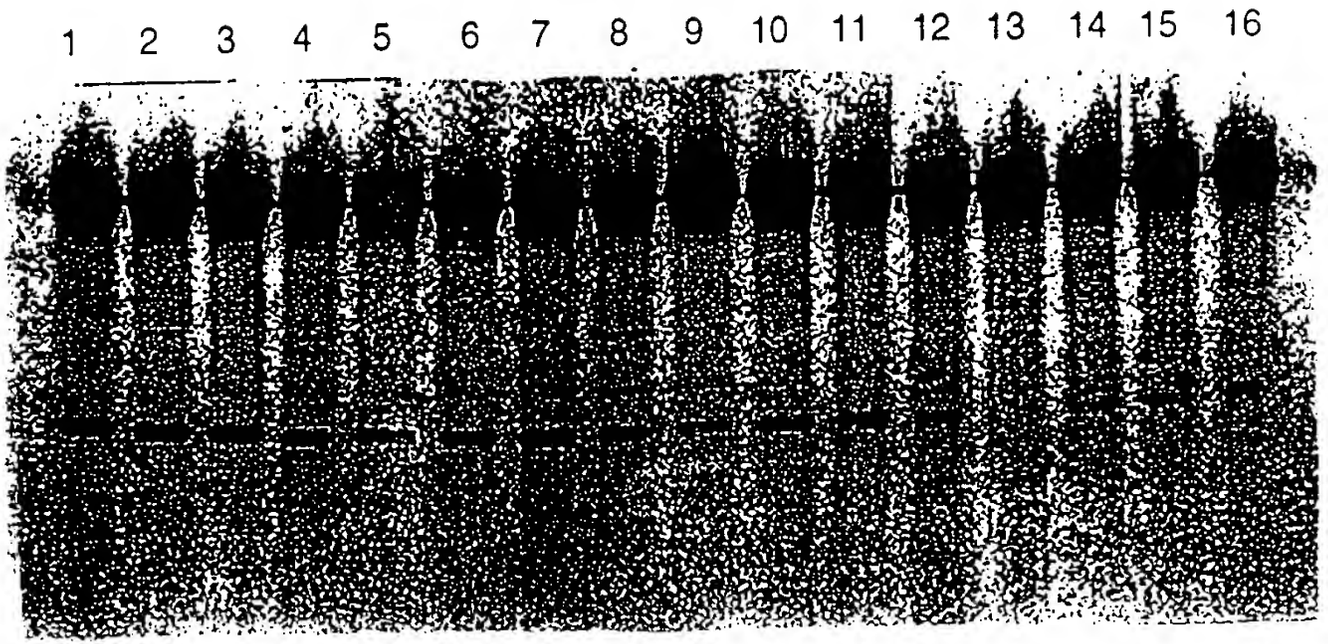


FIG. 45

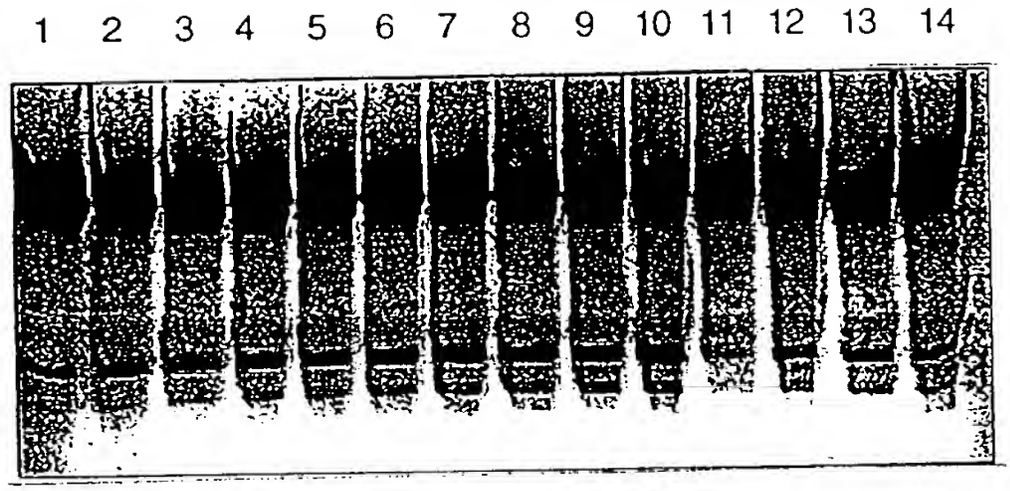


FIG. 46

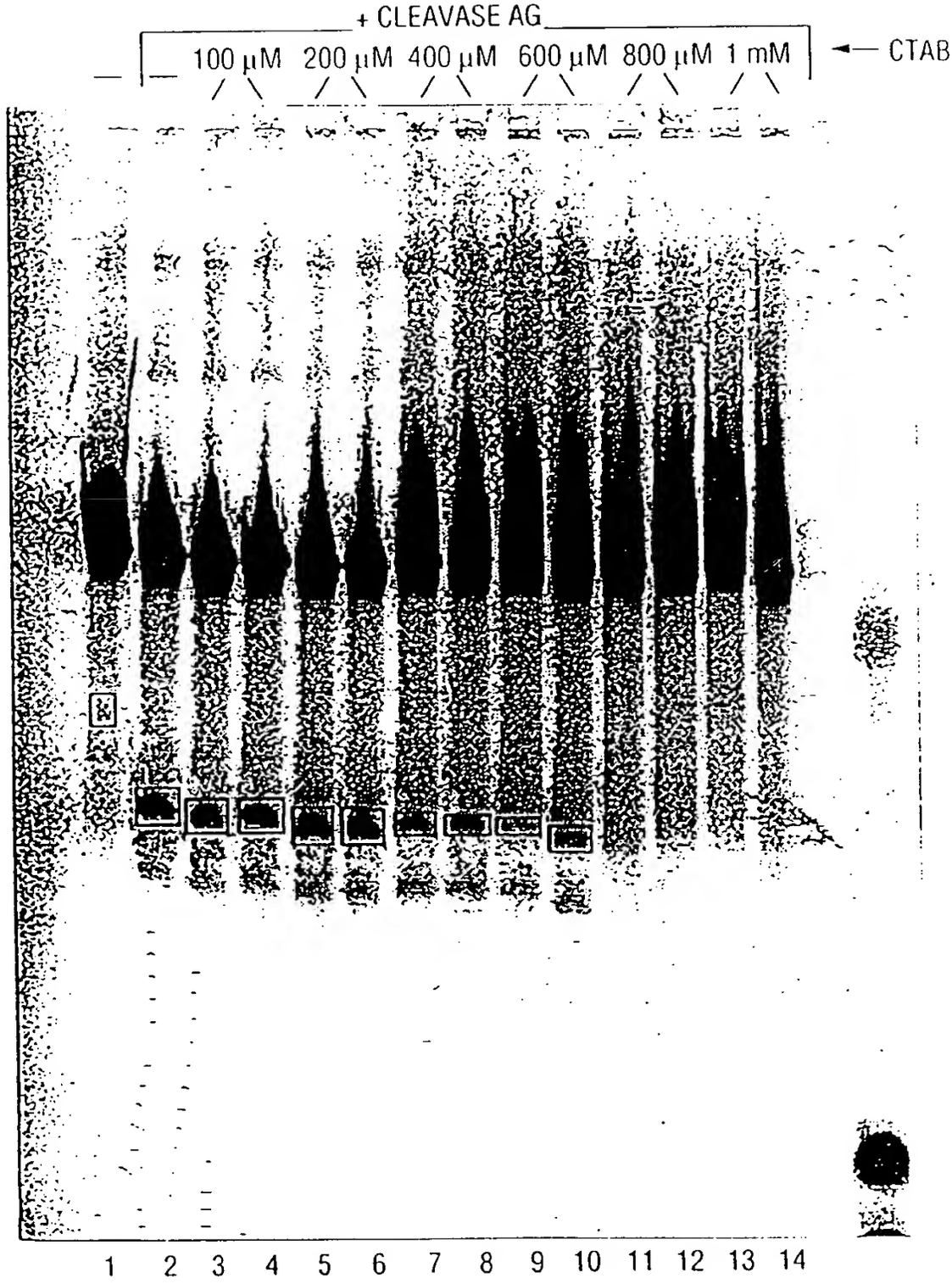

+ CLEAVASE AG
100 µM
200 µM
400 µM
600 µM
800 µM
1 mM
CTAB
1
2
3
4
5
6
7
8
9
10
11
12
13
14

FIG. 47

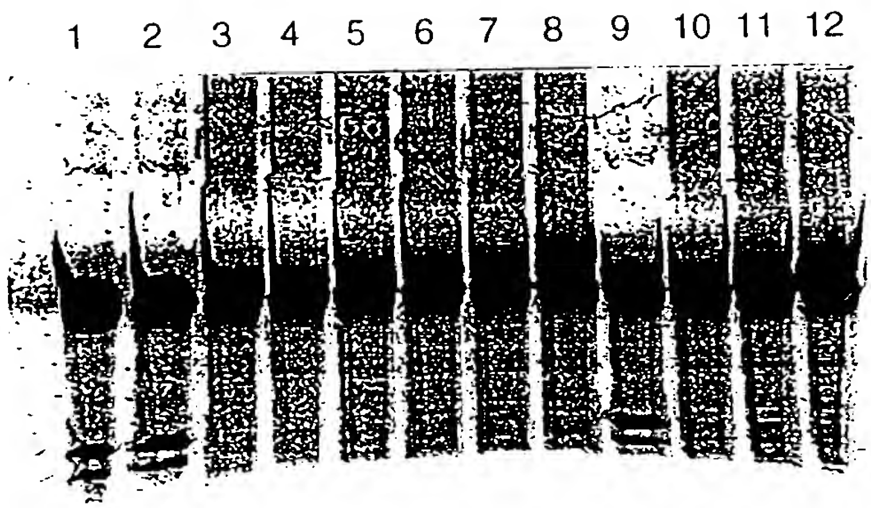


FIG. 48

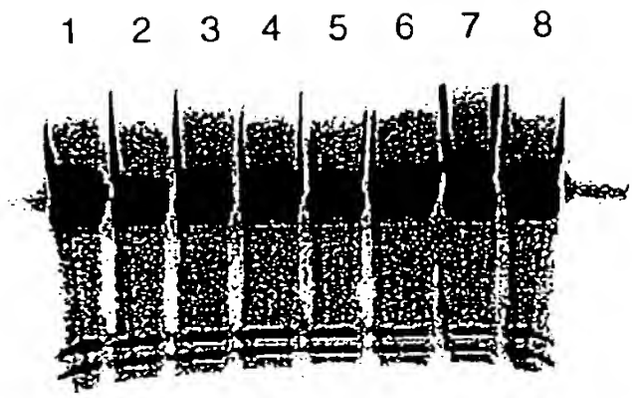


FIG. 49

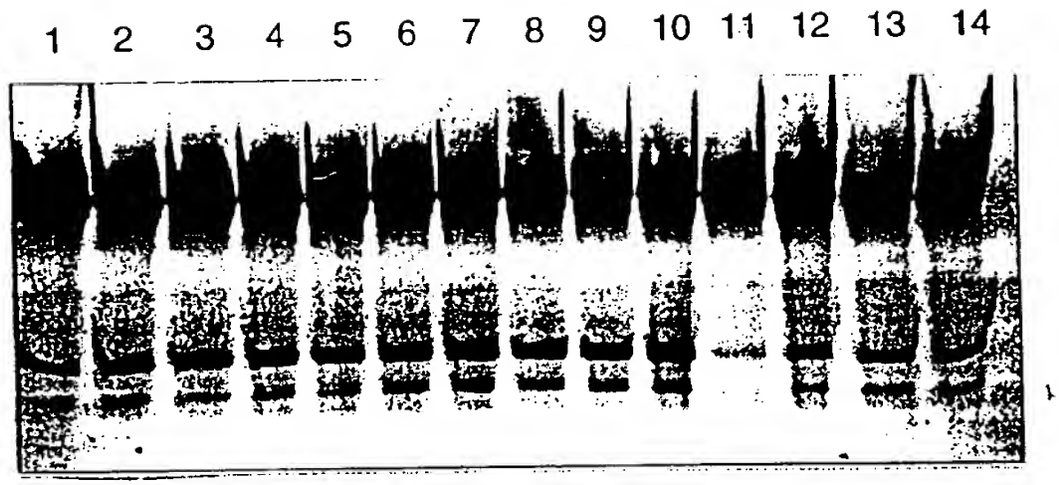


FIG. 50

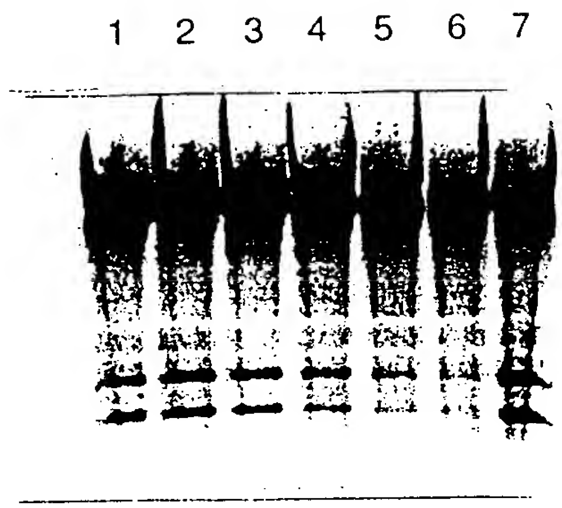


FIG. 51

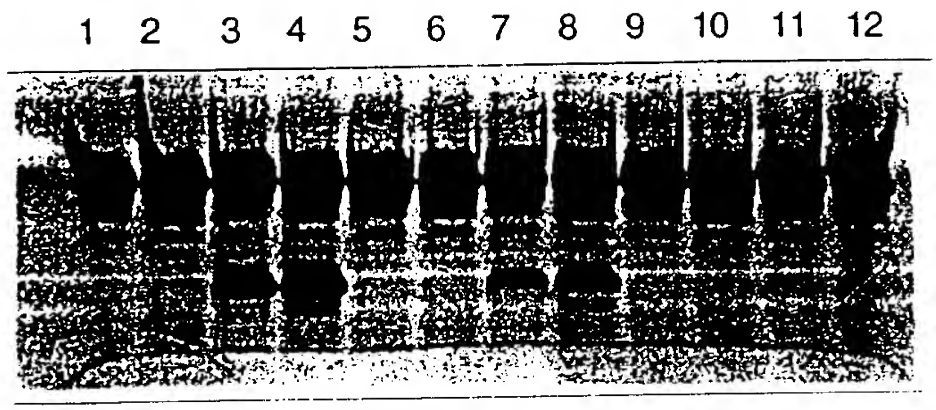


FIG. 52

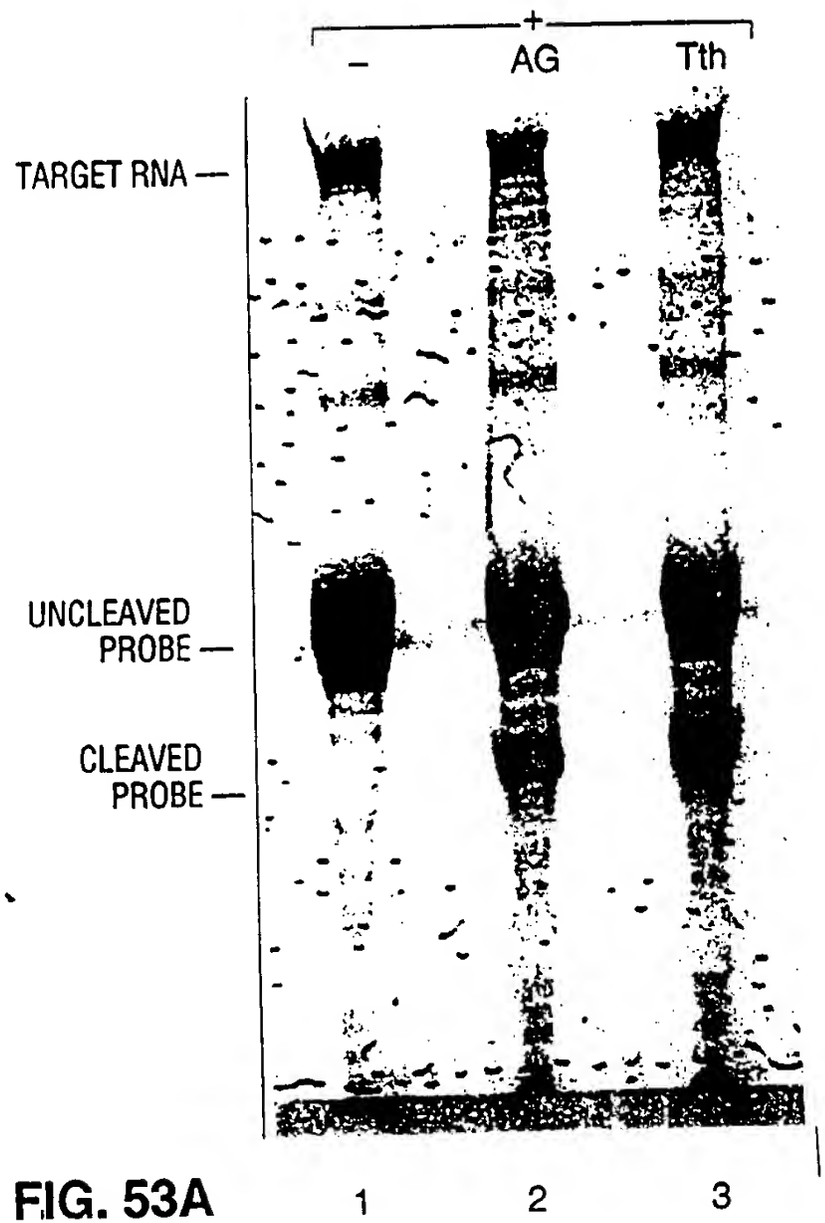


FIG. 53A

FIG. 53B

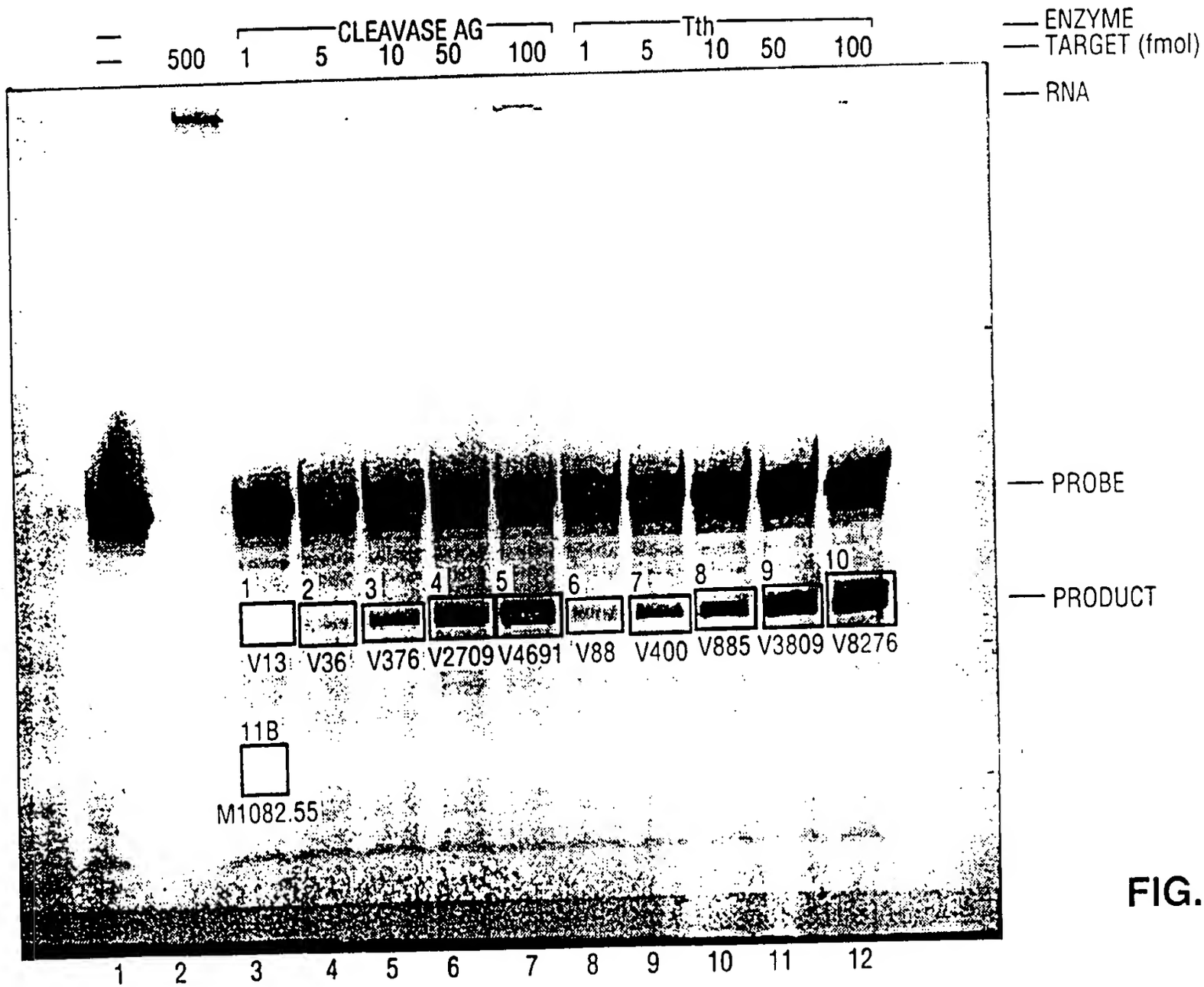

ENZYME
TARGET (fmol)
RNA
CLEAVASE AG
Tth
500
1
5
10
50
100
1
5
10
50
100
PROBE
PRODUCT
1
2
3
4
5
6
7
8
9
10
V13
V36
V376
V2709
V4691
V88
V400
V885
V3809
V8276
11B
M1082.55
1
2
3
4
5
6
7
8
9
10
11
12

FIG. 54

FIG. 55

70 (C10 amino T's)
74 (C6 amino T's)

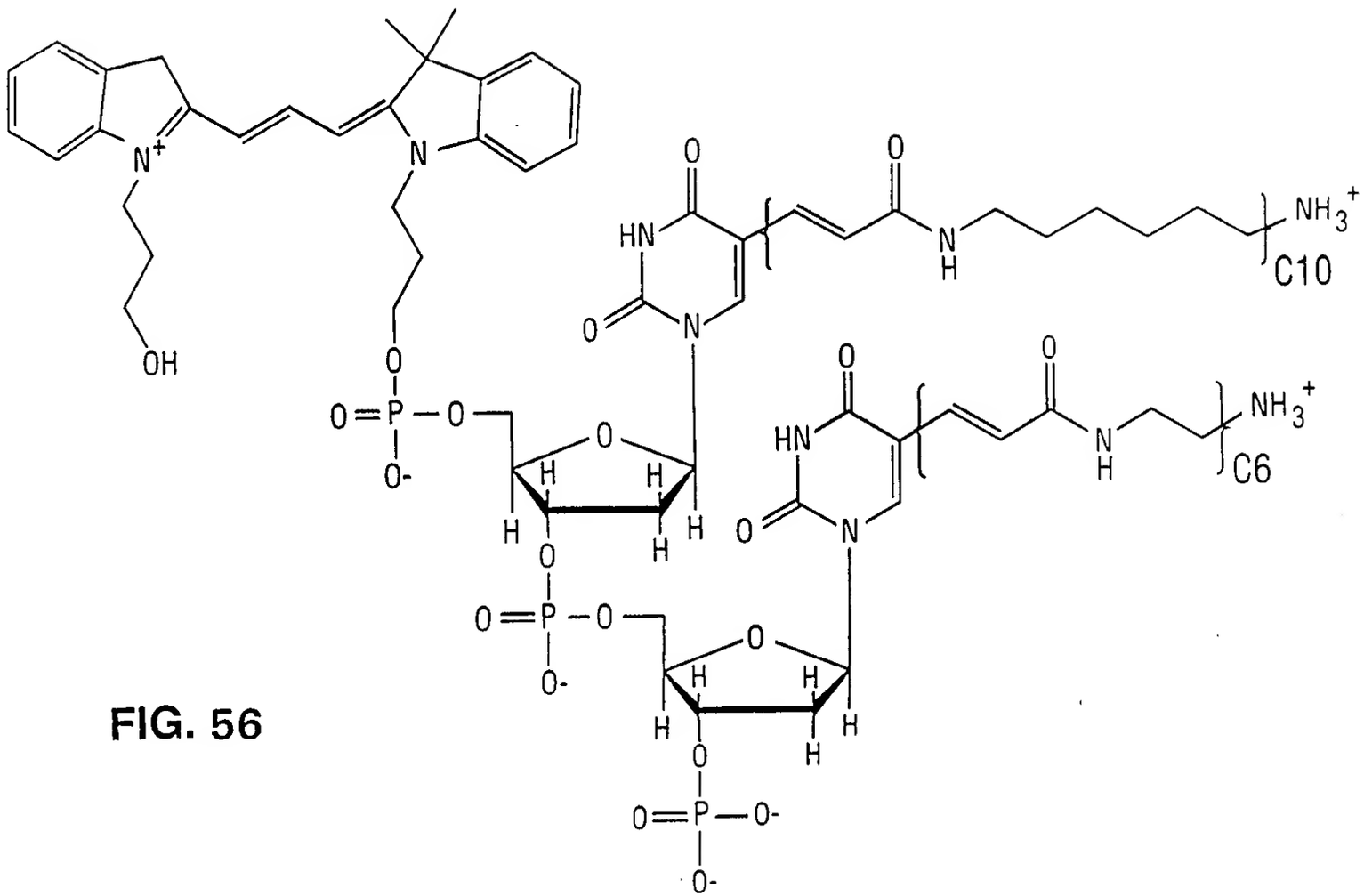


FIG. 56

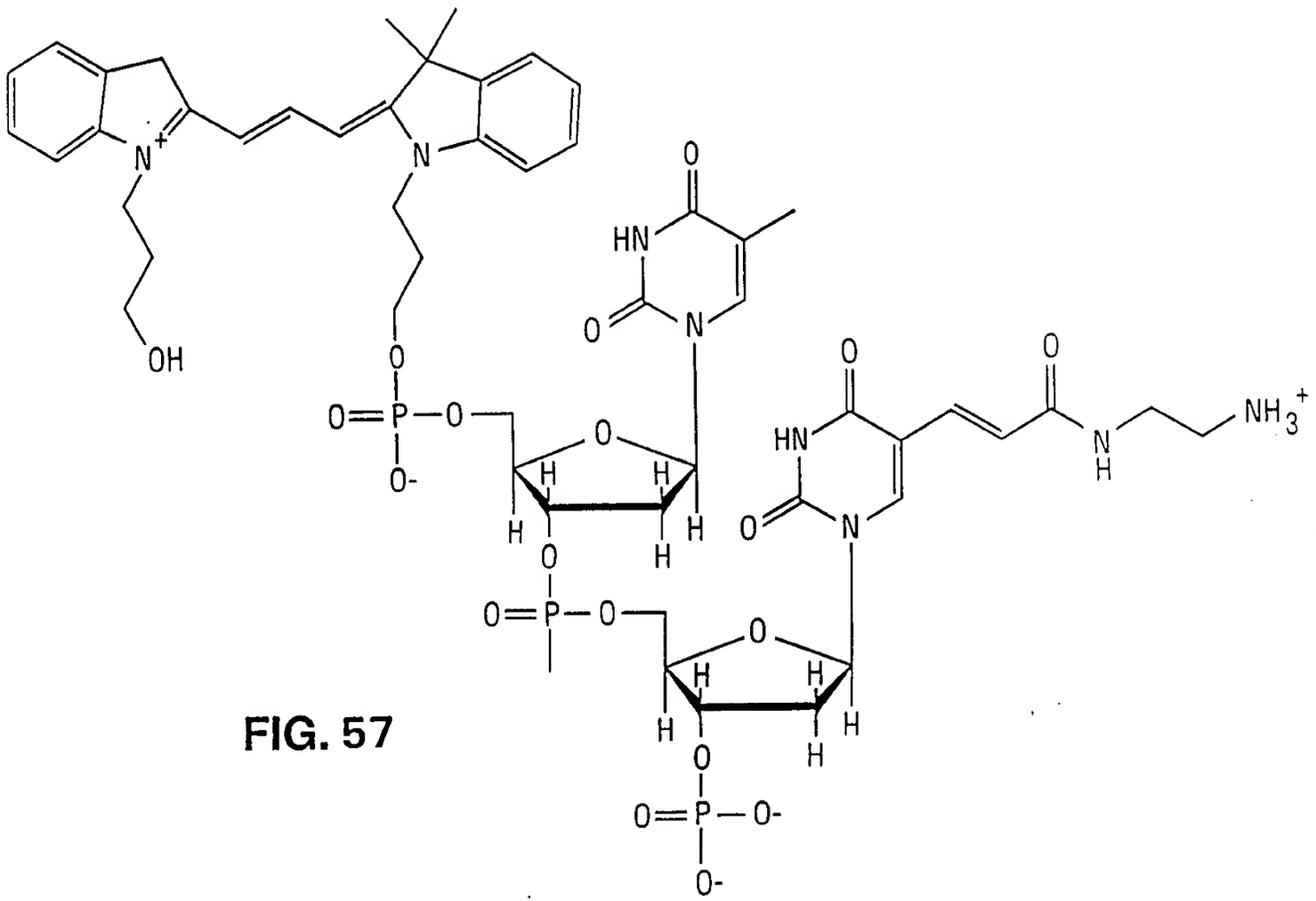


FIG. 57

76

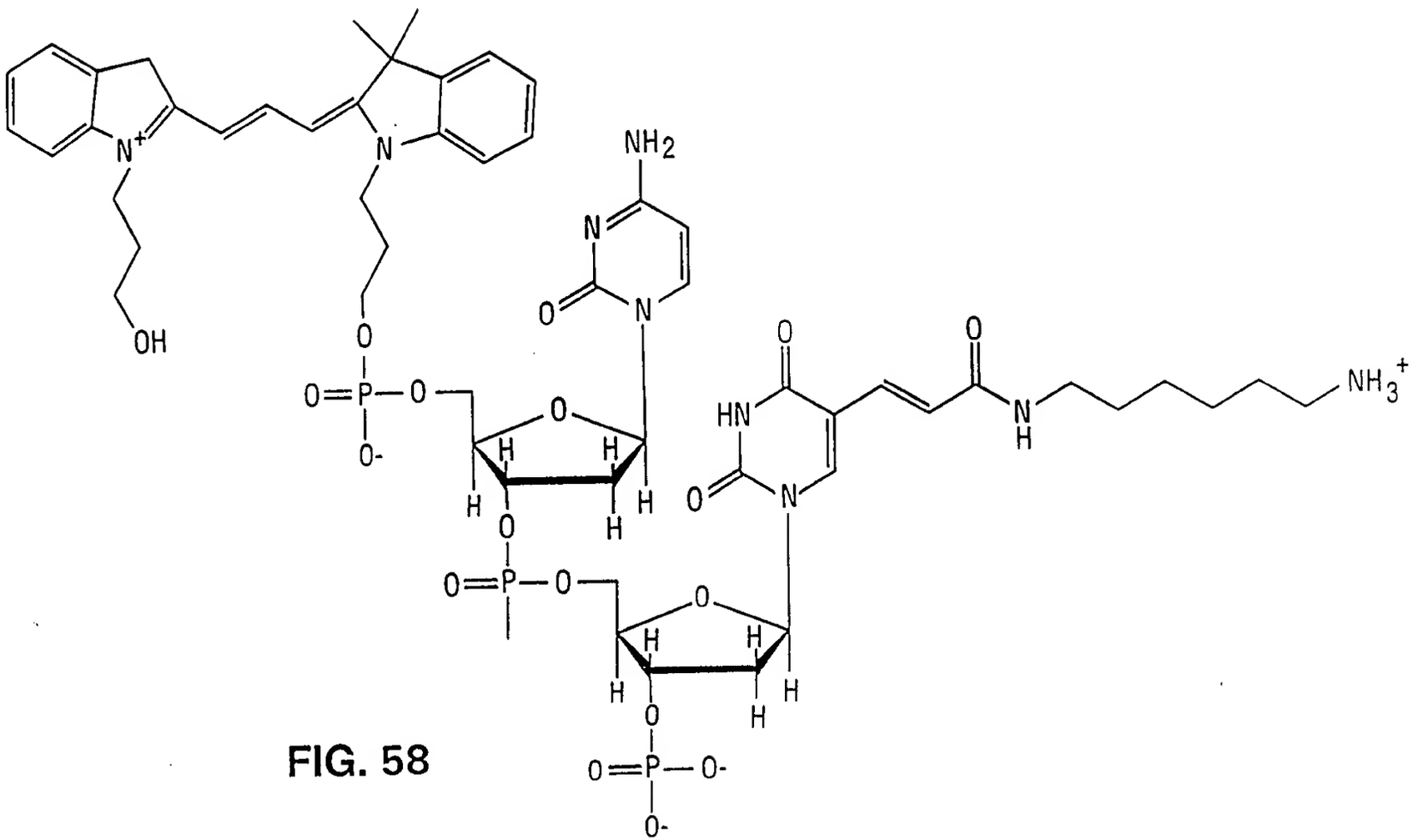


FIG. 58

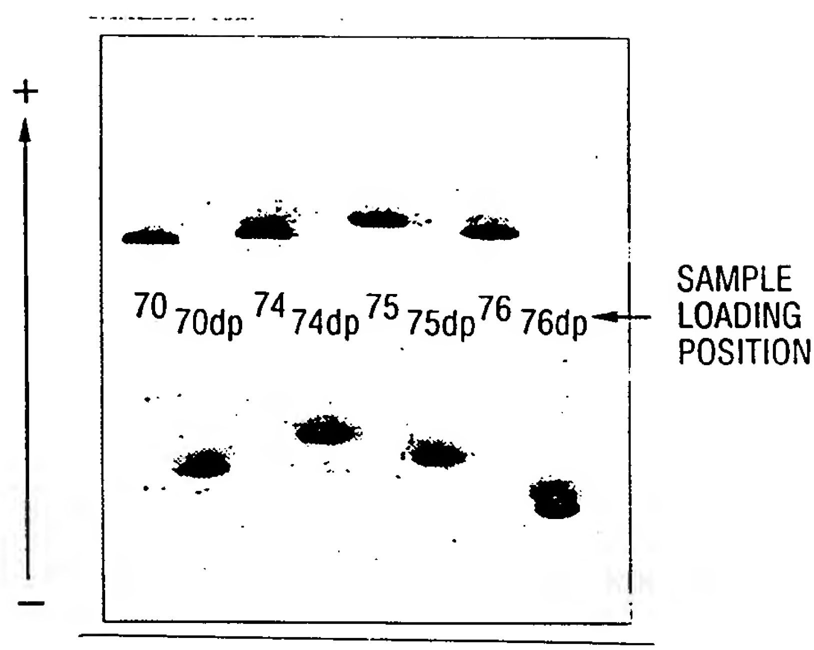


FIG. 59

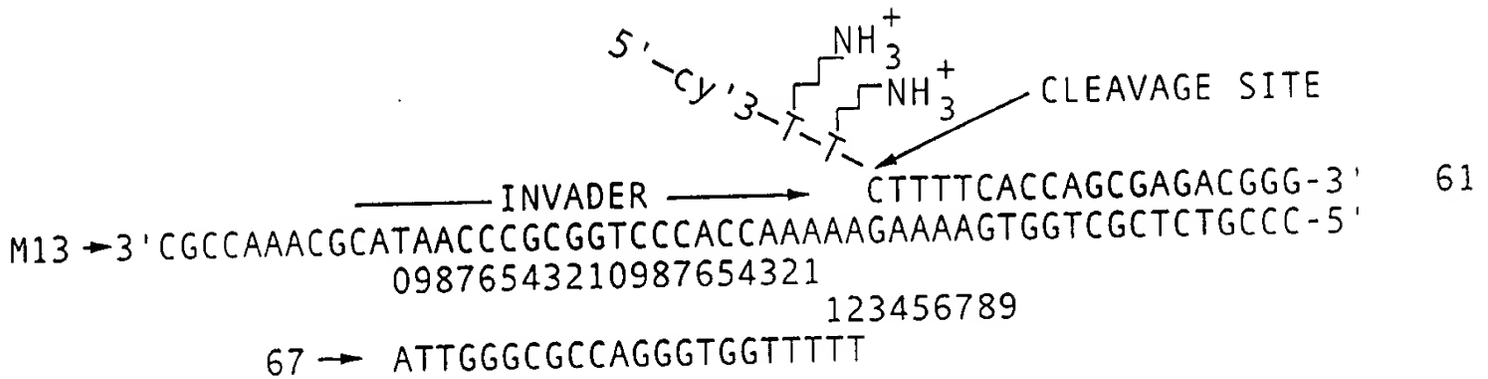

5'-Cy-3'
NH3+
NH3+
CLEAVAGE SITE
INVADER
CTTTTCACCAGCGAGACGGG-3'
61
M13 3'CGCCAAACGCATAACCCGCGGTCCCACCAAAAAGAAAAGTGGTCGCTCTGCCC-5'
09876543210987654321
123456789
67 ATTGGGCGCCAGGGTGGTTTTT

FIG. 60A

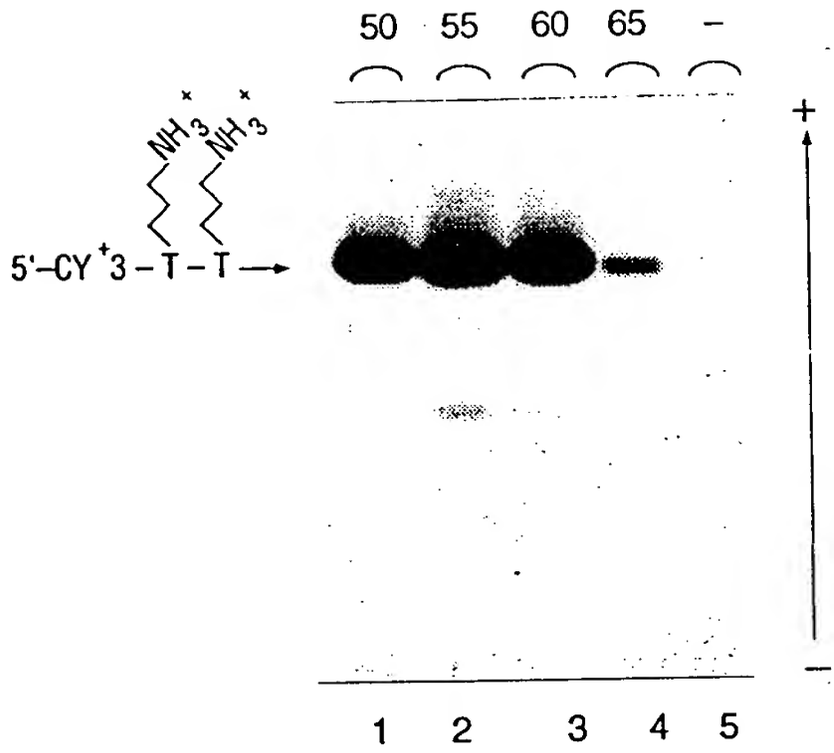


FIG. 60B

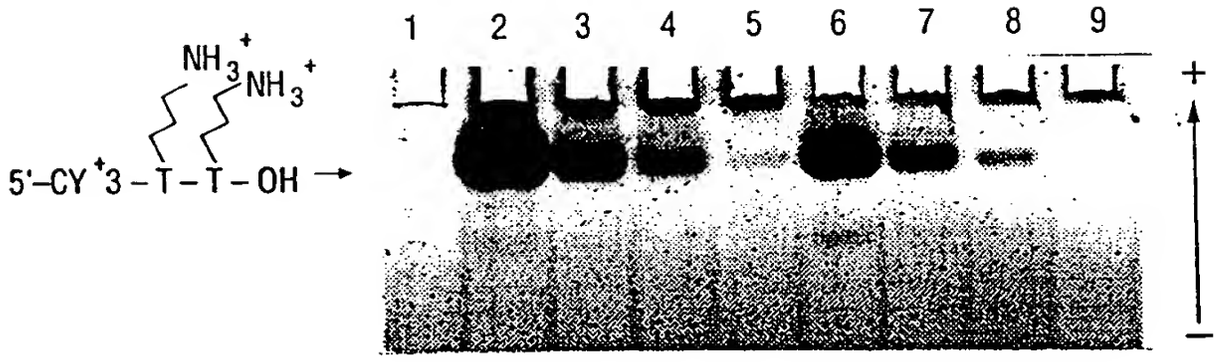


FIG. 61

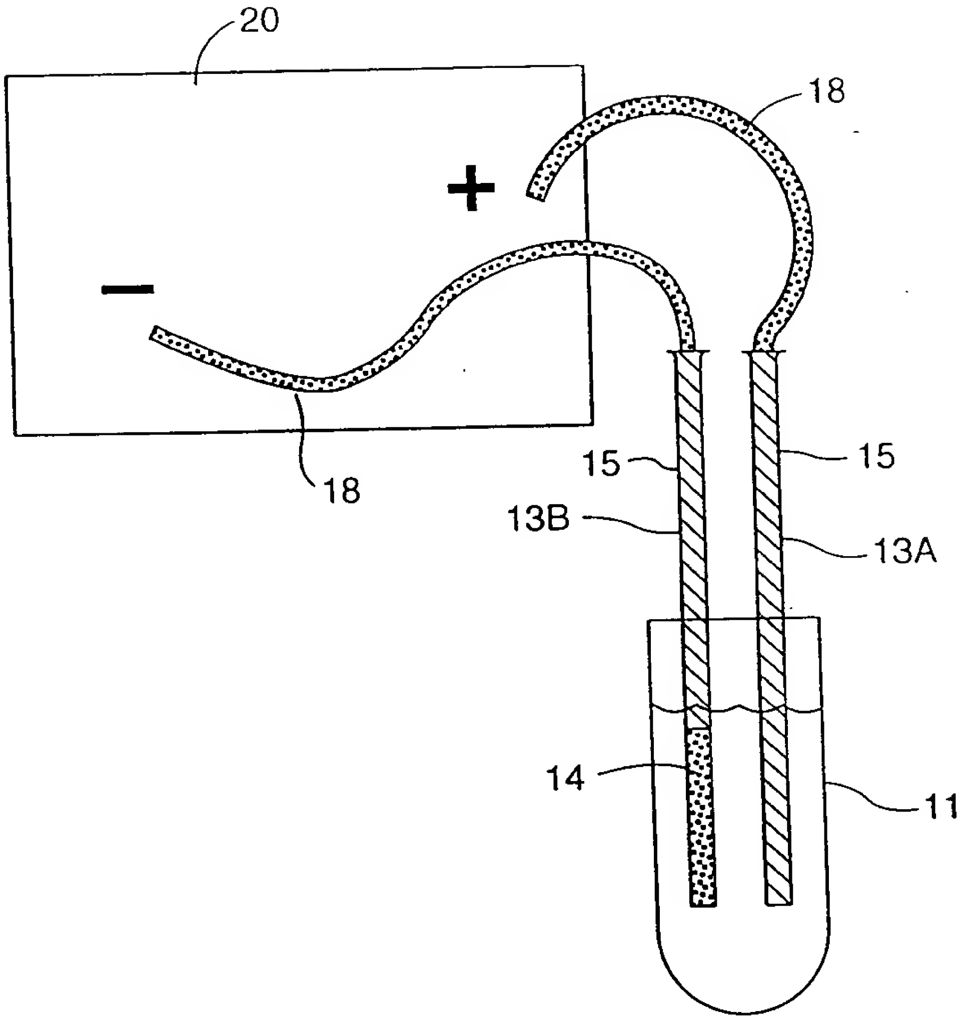


FIG. 62

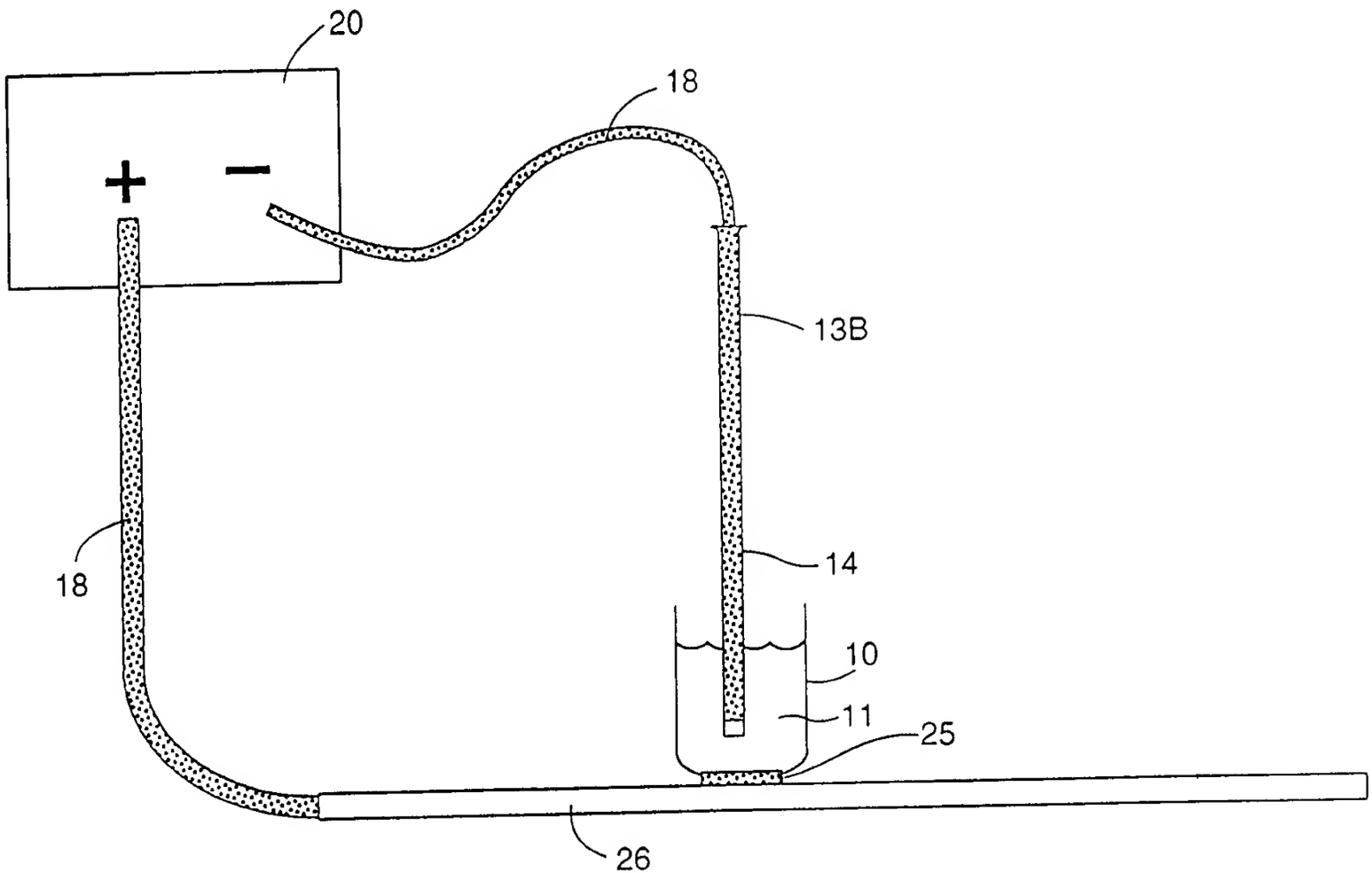


FIG. 63

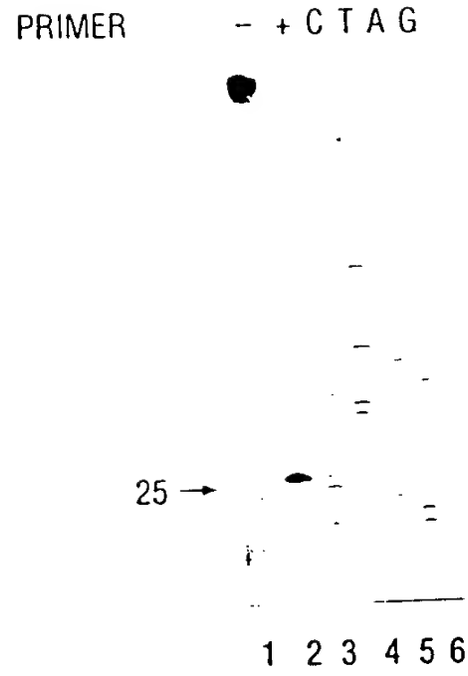


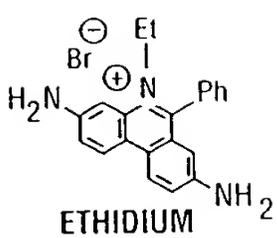
FIG. 64

FIG. 65A

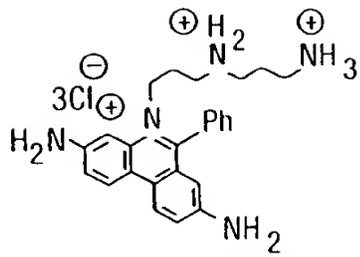
FIG. 65B

FIG. 65C

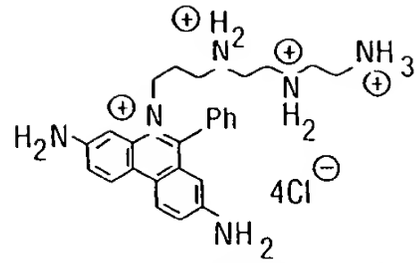
FIG. 65D



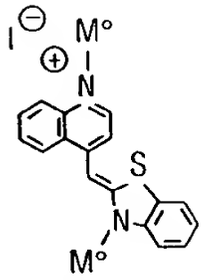
ETHIDIUM BROMIDE



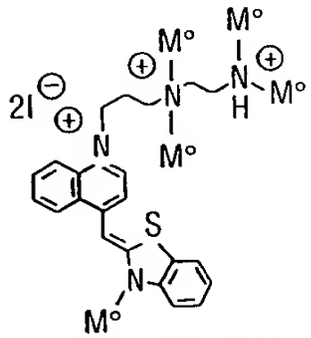
(1,3-PROPANEDIAMINO)-PROPIDIUM



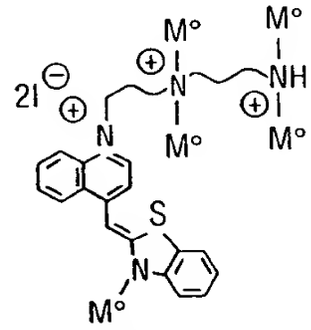
(DIETHYLENETRIAMINO)-PROPIDIUM



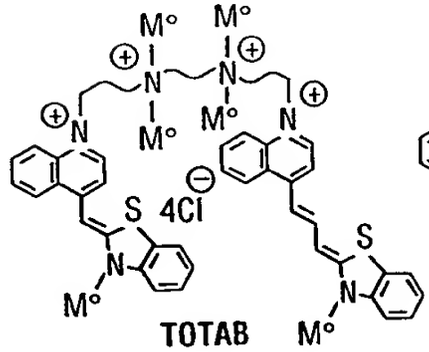
THIAZOLE ORANGE



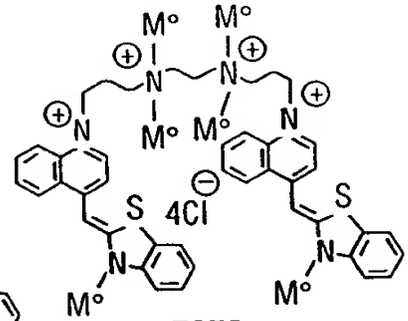
(N-N'-TETRAMETHYL-1,2-ETHANEDIAMINO)-PROPYL THIAZOLE ORANGE



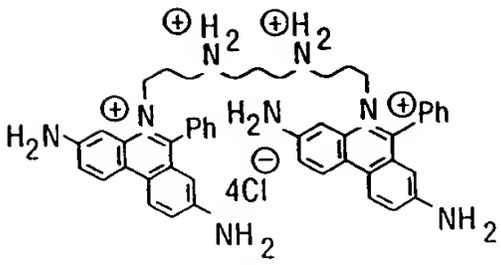
(N-N'-TETRAMETHYL-1,3-PROPANEDIAMINO)-PROPYL THIAZOLE ORANGE



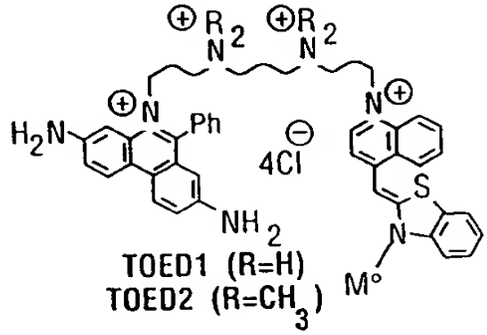
TOTAB



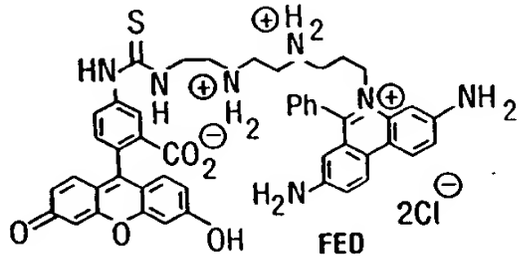
TOTO



EthD



TOED1 (R=H)
TOED2 ($R=CH_3$)



FED

FIG. 66

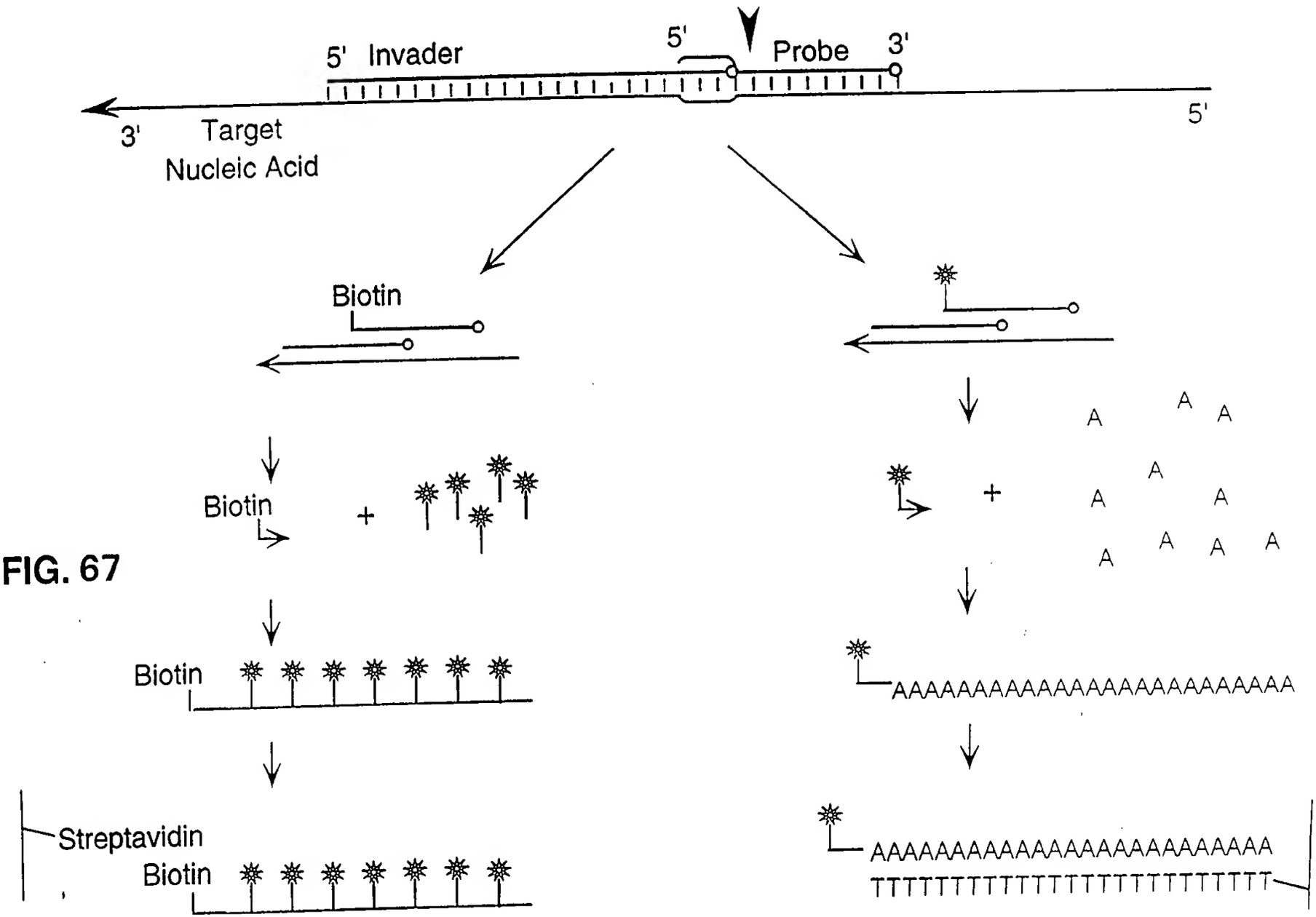

5' Invader
5'
Probe
3'
3'
Target
Nucleic Acid
5'
Biotin
Biotin
+
Biotin
Streptavidin
Biotin
A
A
A
A
A
A
A
A
A
+
AAAAAAAAAAAAAAAAAAAAAAAAA
AAAAAAAAAAAAAAAAAAAAAAAAA
TTTTTTTTTTTTTTTTTTTTTTTTT

FIG. 67

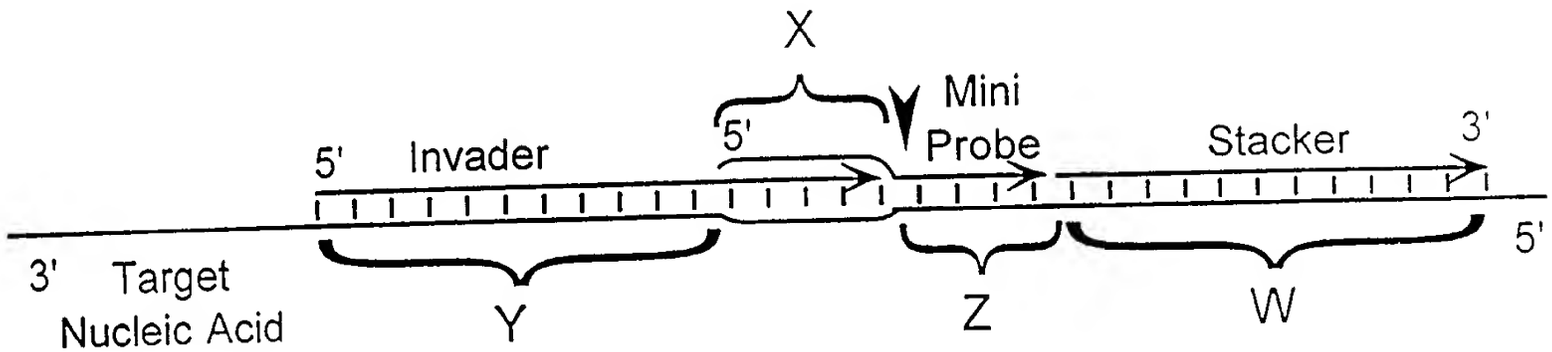


FIG. 68

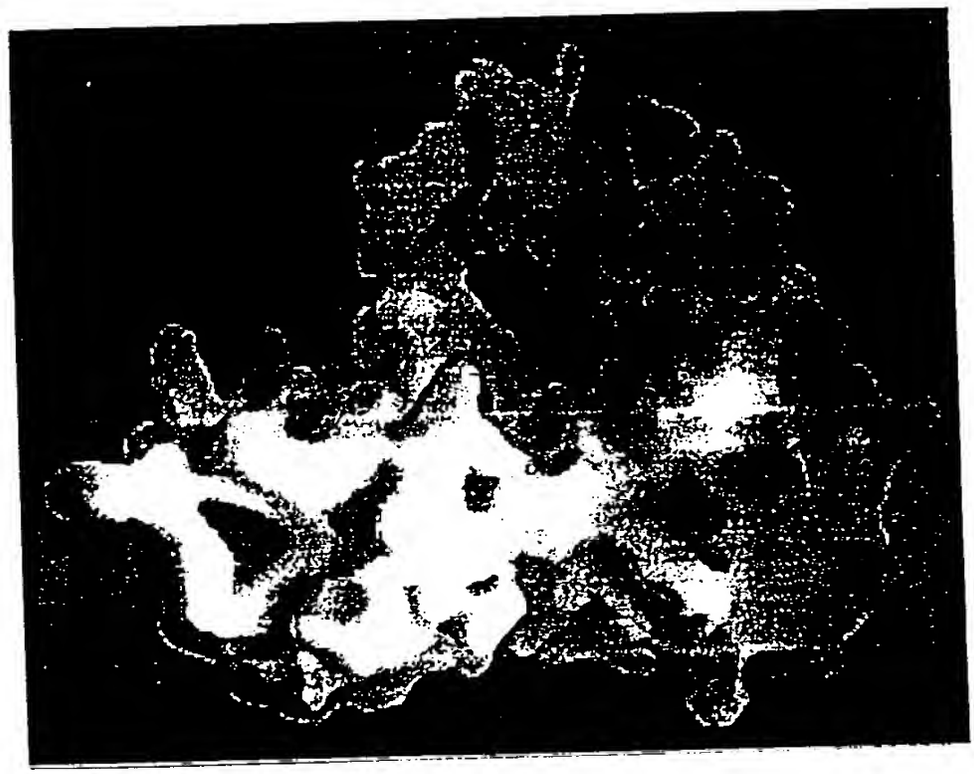


FIG. 69

```
            10        20        30        40        50        60        70
1  MGVQ-----FGDFIPK--NIISFEDLKGKKVAIDGMNALYQFLTSIRLRDGSPLRNRKGEITSAYNGVFY MJAFEN1.PRO
1  MGVP-----IGEIIPR--KEIELENLYGKKIAIDALNAIYQFLSTIRQKDGTPLMDSKGRITSHLSGLFY PFUFEN1.PRO
1  MGIQGLAKLIADVAPSAIRENDIKSYFGRKVAIDASMSIYQFLIAVRQ-GGDVLQNEEGETTSHLMGMFY HUMFEN1.PRO
1  MGIHGLAKLIADVAPSAIRENDIKSYFGRKVAIDASMSIYQFLIAVRQ-GGDVLQNEEGETTS-LMGMFY MUSFEN1.PRO
1  MGIKGLNAIISEHVPSAIRKSDIKSFFGRKVAIDASMSLYQFLIAVRQQDGGQLTNEAGETTSHLMGMFY YST510.PRO
1  MGVHSFWDIAG----PTARPVRLESLEDKRMAVDASIWIYQFLKAVRDQEGNAVKN------SHITGFFR YSTRAD2.PRO
1  MGVSGLWNILE----PVKRPVKLETLVNKRLAIDASIWIYQFLKAVRDKEGNQLKS------SHVVGFFR SPORAD13.PRO
1  MGVQGLWKLLE----CSGROVSPEALEGKILAVDISIWLNQALKGVRDRHGNSIEN------PHLLTLFH HUMXPG.PRO
1  MGVQGLWKLLE----CSGHRVSPEALEGKVLAVDISIWLNQALKGVRDSHGNVIEN------AHLLTLFH MUSXPG.PRO
1  MGVQGLWKLLE----CSGRPINPGTLEGKILAVDISIWLNQAVKGARDRQGNAIQN------AHLLTLFH XENXPG.PRO
1  MTINGIWEWANHVV----RKVPNETMRDKTLSIDGHIWLYESLKGCEAHHQQT-------PNSYLVTFFT CELRAD2.PRO

            80        90       100       110       120       130       140
64 KTIHLLENDITPIWVFDGEPPKLKEKTRKVRREMKEKAELKMKEAIKK----EDFEEAAKYAKRVSYLTP MJAFEN1.PRO
64 RTINLMEAGIKPVYVFDGEPPEFKKKELEKRREAREEAEEKWREALEK----GEIEEARKYAQRATRVNE PFUFEN1.PRO
70 RTIRMMENGIKPVYVFDGKPPQLKSGELAKRSERRAEAEKQLQQAQAA----GAEOEVEKFTKRLVKVTK HUMFEN1.PRO
69 RTIRM-ENGIKPVYVFDGKPPQLKSGELAKRSERRAEAEKQLQQAQEA----GMEEEVEKFTKRLVKVTK MUSFEN1.PRO
71 RTLRMIDNGIKPCYVFDGKPPDLKSHELTKRSSRRVETEKKLA---EA----TTELEKMKQERRLVKVSK YST510.PRO
61 RICKLLYFGIRPVFVFDGGVPVLKRETIRQRKERRQGKRESAKSTARKLLALQLQNGSNDNKRDSDEVTM YSTRAD2.PRO
61 RICKLLFFGIKPVFVFDGGAPSLKRQTIQKRQARRLDREENATVTANKLLALQMRHQAMLLKRDADEVTQ SPORAD13.PRO
61 RLCKLLFFRIRPIFVFDGDAPLLKKQTLVKRRQRKDLASSDSRKTTEKLLKTFLKRQAIKTERIAATVTG HUMXPG.PRO
61 RLCKLLFFRIRPIFVFDGDAPLLKKQTLAKRRQRKDSASIDSRKTTEKLLKTFLKRQALKTDRIAASVTG MUSXPG.PRO
61 RLCKLLFFRIRPIFVFDGEAPLLKRQTLAKRRQRTDKASNDARKTNEKLLRTFLKRQAIKAERIAATVTG XENXPG.PRO
60 RIQRLLELKIIPIVVFDNINASSSAHESKDQNEFVPRKRRSFGDSPFTNLV------------------- CELRAD2.PRO
```

FIG. 70A

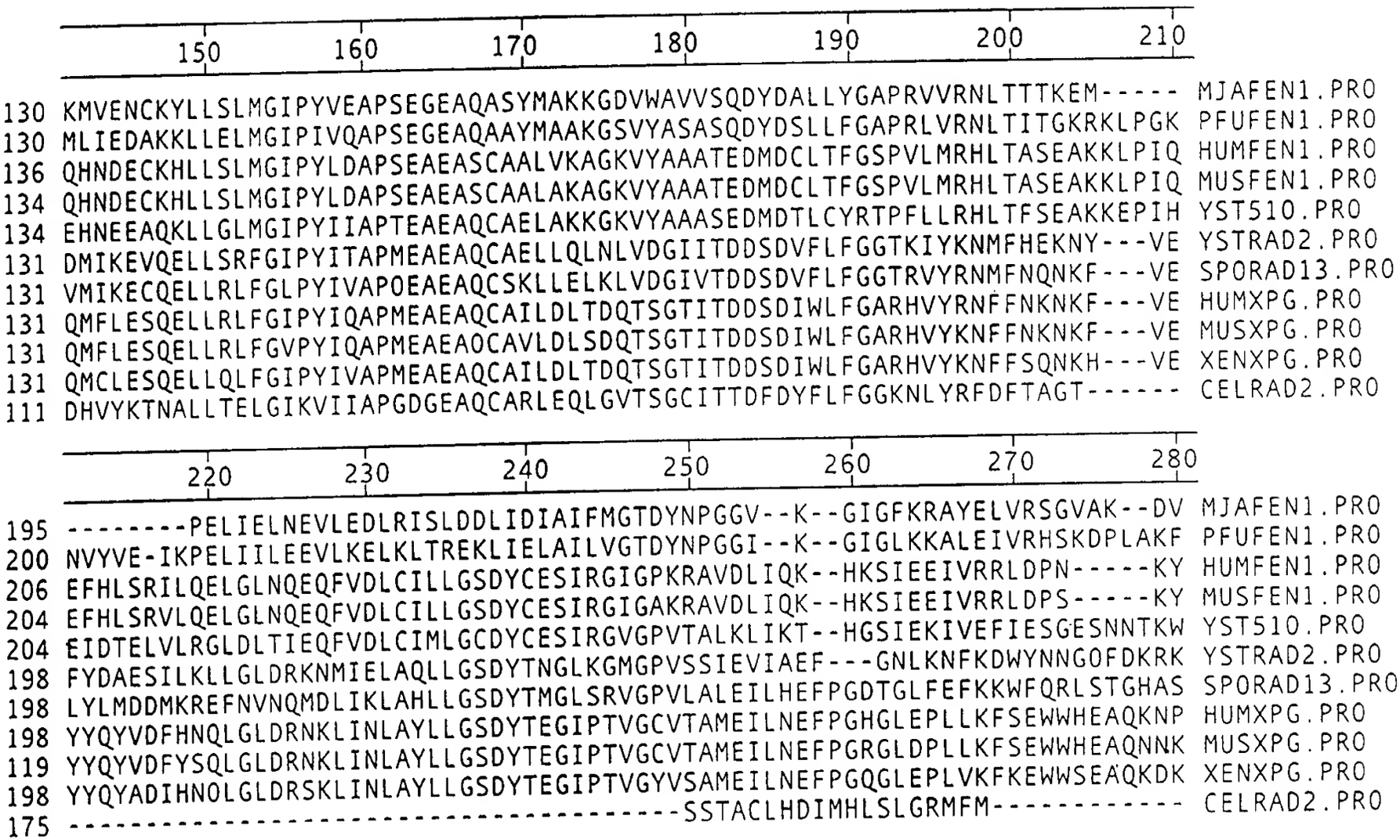

150 160 170 180 190 200 210
130 KMVENCKYLLSLMGIPYVEAPSEGEAQASYMAKKGDVWAVVSQDYDALLYGAPRVVRNLTTTKEM----- MJAFEN1.PRO
130 MLIEDAKKLLELMGIPIVQAPSEGEAQAAYMAAKGSVYASASQDYDSLLFGAPRLVRNLTITGKRKLPGK PFUFEN1.PRO
136 QHNDECKHLLSLMGIPYLDAPSEAEASCAALVKAGKVYAAATEDMDCLTFGSPVLMRHLTASEAKKLPIQ HUMFEN1.PRO
134 QHNDECKHLLSLMGIPYLDAPSEAEASCAALAKAGKVYAAATEDMDCLTFGSPVLMRHLTASEAKKLPIQ MUSFEN1.PRO
134 EHNEEAQKLLGLMGIPYIIAPTEAEAQCAELAKKGKVYAAASEDMDTLCYRTPFLLRHLTFSEAKKEPIH YST510.PRO
131 DMIKEVQELLSRFGIPYITAPMEAEAQCAELLQLNLVDGIITDDSDVFLFGGTKIYKNMFHEKNY---VE YSTRAD2.PRO
131 VMIKECQELLRLFGLPYIVAPOEAEAQCSKLLELKLVDGIVTDDSDVFLFGGTRVYRNMFNQNKF---VE SPORAD13.PRO
131 QMFLESQELLRLFGIPYIQAPMEAEAQCAILDLTDQTSGTITDDSDIWLFGARHVYRNFFNKNKF---VE HUMXPG.PRO
131 QMFLESQELLRLFGIPYIQAPMEAEAQCAVLDLSDQTSGTITDDSDIWLFGARHVYKNFFNKNKF---VE MUSXPG.PRO
131 QMCLESQELLQLFGIPYIVAPMEAEAQCAILDLTDQTSGTITDDSDIWLFGARHVYKNFFSQNKH---VE XENXPG.PRO
111 DHVYKTNALLTELGIKVIIAPGDGEAQCARLEQLGVTSGCITTDFDYFLFGGKNLYRFDFTAGT------ CELRAD2.PRO
220 230 240 250 260 270 280
195 --------PELIELNEVLEDLRISLDDLIDIAIFMGTDYNPGGV--K--GIGFKRAYELVRSGVAK--DV MJAFEN1.PRO
200 NVYVE-IKPELIILEEVLKELKLTREKLIELAILVGTDYNPGGI--K--GIGLKKALEIVRHSKDPLAKF PFUFEN1.PRO
206 EFHLSRILQELGLNQEQFVDLCILLGSDYCESIRGIGPKRAVDLIQK--HKSIEEIVRRLDPN-----KY HUMFEN1.PRO
204 EFHLSRVLQELGLNQEQFVDLCILLGSDYCESIRGIGAKRAVDLIQK--HKSIEEIVRRLDPS-----KY MUSFEN1.PRO
204 EIDTELVLRGLDLTIEQFVDLCIMLGCDYCESIRGVGPVTALKLIKT--HGSIEKIVEFIESGESNNTKW YST510.PRO
198 FYDAESILKLLGLDRKNMIELAQLLGSDYTNGLKGMGPVSSIEVIAEF---GNLKNFKDWYNNGQFDKRK YSTRAD2.PRO
198 LYLMDDMKREFNVNQMDLIKLAHLLGSDYTMGLSRVGPVLALEILHEFPGDTGLFEFKKWFQRLSTGHAS SPORAD13.PRO
198 YYQYVDFHNQLGLDRNKLINLAYLLGSDYTEGIPTVGCVTAMEILNEFPGHGLEPLLKFSEWWHEAQKNP HUMXPG.PRO
198 YYQYVDFYSQLGLDRNKLINLAYLLGSDYTEGIPTVGCVTAMEILNEFPGRGLDPLLKFSEWWHEAQNNK MUSXPG.PRO
119 YYQYVDFYSQLGLDRNKLINLAYLLGSDYTEGIPTVGYVSAMEILNEFPGQGLEPLVKFKEWWSEAQKDK XENXPG.PRO
198 YYQYADIHNQLGLDRSKLINLAYLLGSDYTEGIPTVGYVSAMEILNEFPGQGLEPLVKFKEWWSEAQKDK ----------
175 ----------SSTACLHDIMHLSLGRMFM---------- CELRAD2.PRO

FIG. 70B

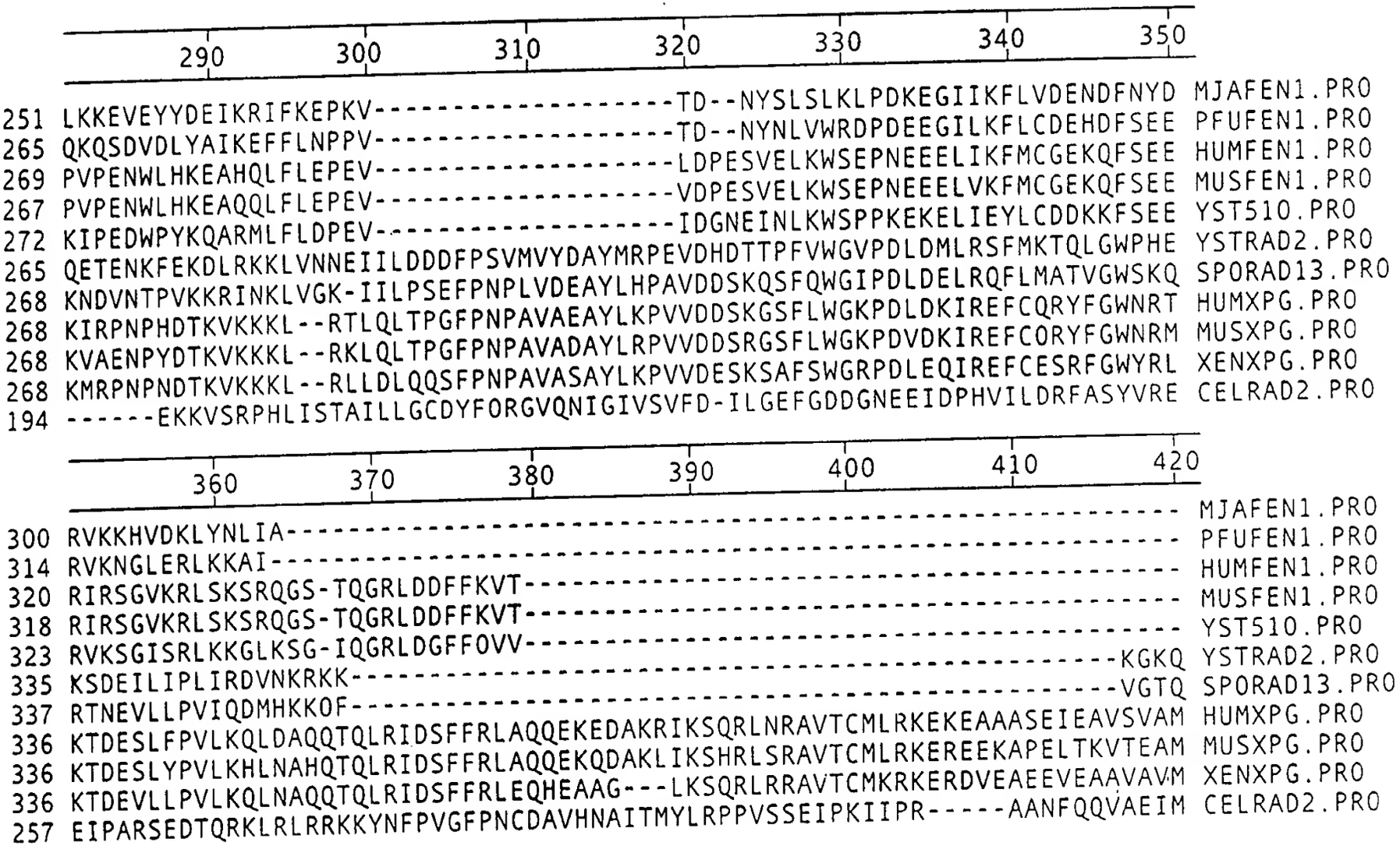

290 300 310 320 330 340 350
251 LKKEVEYYDEIKRIFKEPKV----------TD--NYSLSLKLPDKEGIIKFLVDENDFNYD MJAFEN1.PRO
265 QKQSDVDLYAIKEFFLNPPV----------TD--NYNLVWRDPDEEGILKFLCDEHDFSEE PFUFEN1.PRO
269 PVPENWLHKEAHQLFLEPEV----------LDPESVELKWSEPNEEELIKFMCGEKQFSEE HUMFEN1.PRO
267 PVPENWLHKEAQQLFLEPEV----------VDPESVELKWSEPNEEELVKFMCGEKQFSEE MUSFEN1.PRO
272 KIPEDWPYKQARMLFLDPEV----------IDGNEINLKWSPPKEKELIEYLCDDKKFSEE YST510.PRO
265 QETENKFEKDLRKKLVNNEIILDDDFPSVMVYDAYMRPEVDHDTTPFVWGVPDLDMLRSFMKTQLGWPHE YSTRAD2.PRO
268 KNDVNTPVKKRINKLVGK-IILPSEFPNPLVDEAYLHPAVDDSKQSFQWGIPDLDELRQFLMATVGWSKQ SPORAD13.PRO
268 KIRPNPHDTKVKKKL--RTLQLTPGFPNPAVAEAYLKPVVDDSKGSFLWGKPDLDKIREFCQRYFGWNRT HUMXPG.PRO
268 KIRPNPHDTKVKKKL--RTLQLTPGFPNPAVADAYLRPVVDDSRGSFLWGKPDVDKIREFCQRYFGWNRM MUSXPG.PRO
268 KVAENPYDTKVKKKL--RKLQLTPGFPNPAVADAYLRPVVDDSRGSFLWGKPDLEQIREFCESRFGWYRL XENXPG.PRO
268 KMRPNPNDTKVKKKL--RLLDLQQSFPNPAVASAYLKPVVDESKSAFSWGRPDLEQIREFCESRFGWYRL CELRAD2.PRO
194 ------EKKVSRPHLISTAILLGCDYFORGVQNIGIVSVFD-ILGEFGDDGNEEIDPHVILDRFASYVRE CELRAD2.PRO
360 370 380 390 400 410 420
300 RVKKHVDKLYNLIA---------- MJAFEN1.PRO
314 RVKNGLERLKKAI---------- PFUFEN1.PRO
320 RIRSGVKRLSKSRQGS-TQGRLDDFFKVT---------- HUMFEN1.PRO
318 RIRSGVKRLSKSRQGS-TQGRLDDFFKVT---------- MUSFEN1.PRO
323 RVKSGISRLKKGLKSG-IQGRLDGFFOVV---------- YST510.PRO
335 KSDEILIPLIRDVNKRKK----------KGKQ YSTRAD2.PRO
337 RTNEVLLPVIQDMHKKOF----------VGTQ SPORAD13.PRO
336 KTDESLFPVLKQLDAQQTQLRIDSFFRLAQQEKEDAKRIKSQRLNRAVTCMLRKEKEAAASEIEAVSVAM HUMXPG.PRO
336 KTDESLYPVLKHLNAHQTQLRIDSFFRLAQQEKQDAKLIKSHRLSRAVTCMLRKEREEKAPELTKVTEAM MUSXPG.PRO
336 KTDEVLLPVLKQLNAQQTQLRIDSFFRLEQHEAAG---LKSQRLRRAVTCMKRKERDVEAEEVEAAVAVM XENXPG.PRO
257 EIPARSEDTQRKLRLRRKKYNFPVGFPNCDAVHNAITMYLRPPVSSEIPKIIPR-----AANFQQVAEIM CELRAD2.PRO

FIG. 70C

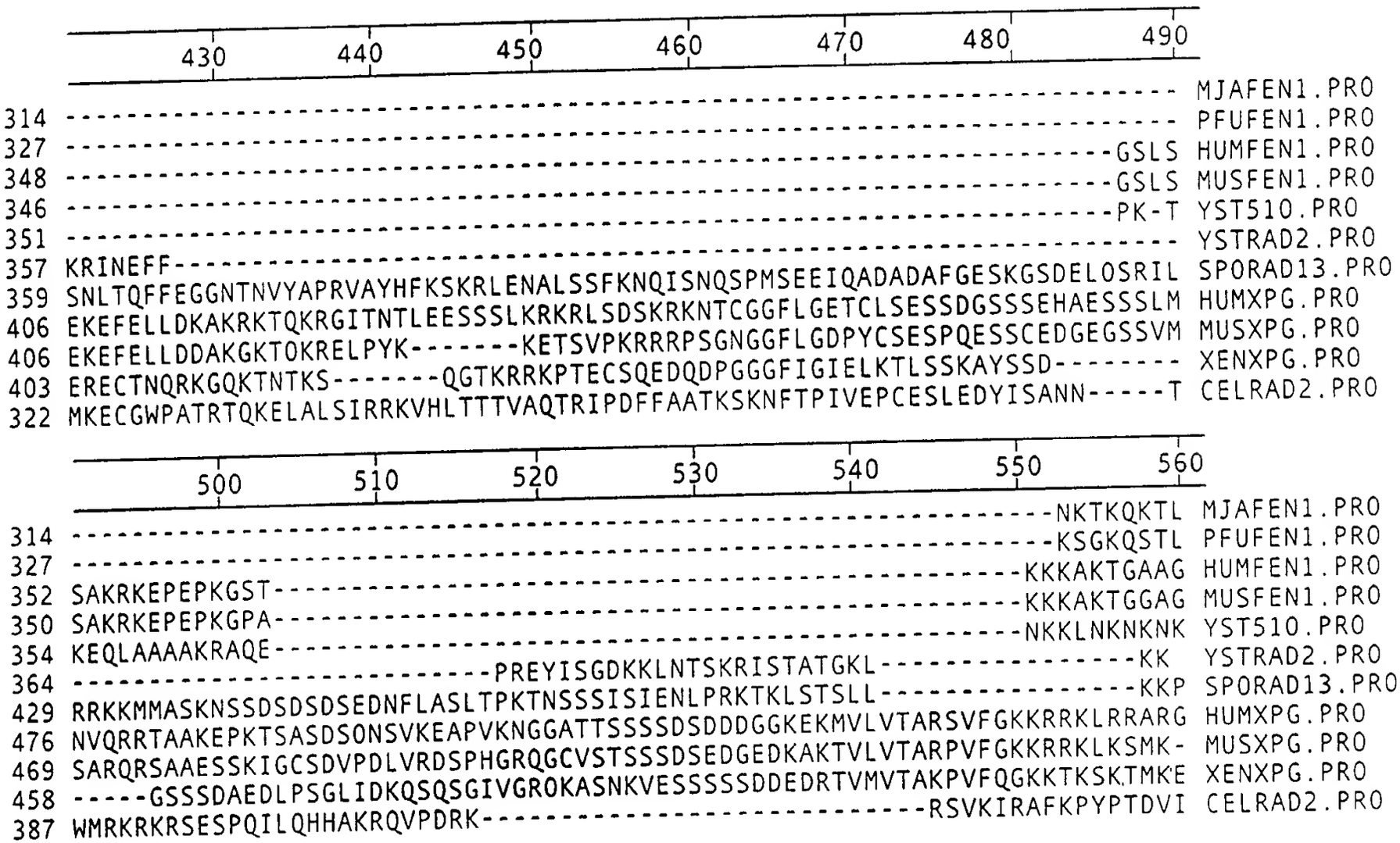

430 440 450 460 470 480 490
MJAFEN1.PRO
314 PFUFEN1.PRO
327 GSLS HUMFEN1.PRO
348 GSLS MUSFEN1.PRO
346 PK-T YST510.PRO
351 YSTRAD2.PRO
357 KRINEFF SPORAD13.PRO
359 SNLTQFFEGGNTNVYAPRVAYHFKSKRLENALSSFKNQISNQSPMSEEIQADADAFGESKGSDELOSRIL HUMXPG.PRO
406 EKEFELLDKAKRKTQKRGITNTLEESSSLKRKRLSDSKRKNTCGGFLGETCLSESSDGSSSEHAESSSLM MUSXPG.PRO
406 EKEFELLDDAKGKTOKRELPYK KETSVPKRRRPSGNGGFLGDPYCSESPQESSCEDGEGSSVM XENXPG.PRO
403 ERECTNQRKGQKTNTKS QGTKRRKPTECSQEDQDPGGGFIGIELKTLSSKAYSSD CELRAD2.PRO
322 MKECGWPATRTQKELALSIRRKVHLTTTVAQTRIPDFFAATKSKNFTPIVEPCESLEDYISANN T
500 510 520 530 540 550 560
NKTKQKTL MJAFEN1.PRO
314 KSGKQSTL PFUFEN1.PRO
327 KKKAKTGAAG HUMFEN1.PRO
352 SAKRKEPEPKGST KKKAKTGGAG MUSFEN1.PRO
350 SAKRKEPEPKGPA NKKLNKNKNK YST510.PRO
354 KEQLAAAAKRAQE KK YSTRAD2.PRO
364 PREYISGDKKLNTSKRISTATGKL KKP SPORAD13.PRO
429 RRKKMMASKNSSDSDSDSEDNFLASLTPKTNSSSISIENLPRKTKLSTSLL KKP HUMXPG.PRO
476 NVQRRTAAKEPKTSASDSONSVKEAPVKNGGATTSSSSDSDDDGGKEKMVLVTARSVFGKKRRKLRRARG MUSXPG.PRO
469 SARQRSAAESSKIGCSDVPDLVRDSPHGRQGCVSTSSSDSEDGEDKAKTVLVTARPVFGKKRRKLKSMK XENXPG.PRO
458 GSSSDAEDLPSGLIDKQSQSGIVGROKASNKVESSSSSDDEDRTVMVTAKPVFQGKKTKSKTMKE CELRAD2.PRO
387 WMRKRKRSESPQILQHHAKRQVPDRK RSVKIRAFKPYPTDVI

FIG. 70D

322	DAWFKZ
335	ESWFKR
375	KFKRGK
373	KFRRGK
377	VTKGRR
390	---RKM
483	SKRRRK
546	RKRKTZ
538	RRKKKT
523	TVKRK
429	ELGDSD

MJAFEN1.PRO
PFUFEN1.PRO
HUMFEN1.PRO
MUSFEN1.PRO
YST510.PRO
YSTRAD2.PRO
SPORAD13.PRO
HUMXPG.PRO
MUSXPG.PRO
XENXPG.PRO
CELRAD2.PRO

FIG. 70E

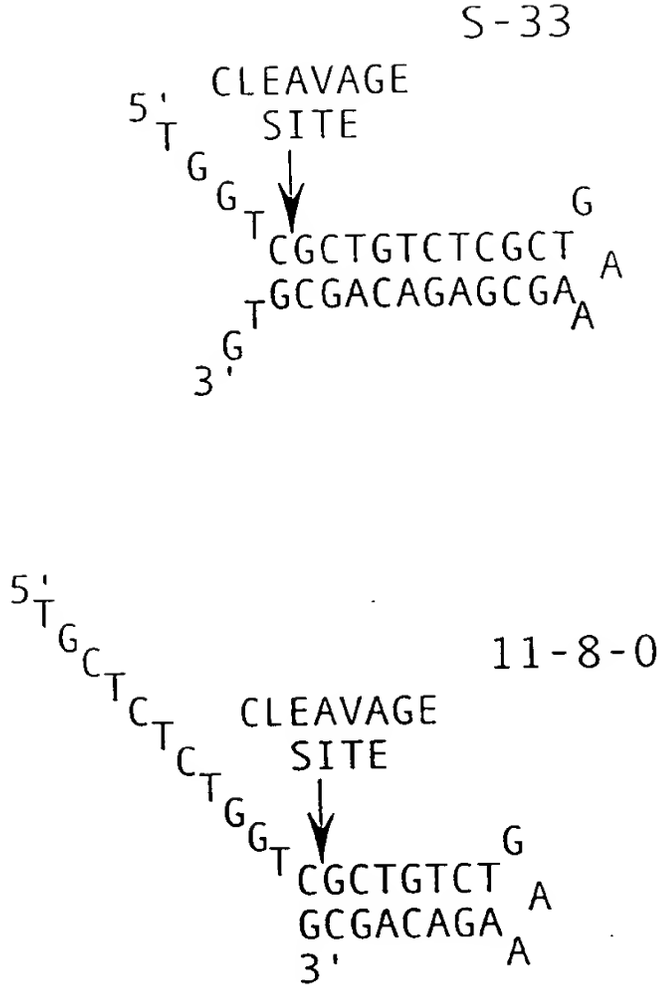


FIG. 71